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New derivatives of hydantoins, thiohydantoins, pyrimidinediones and thioxopyrimidinones, their preparation processes and their use as medicaments

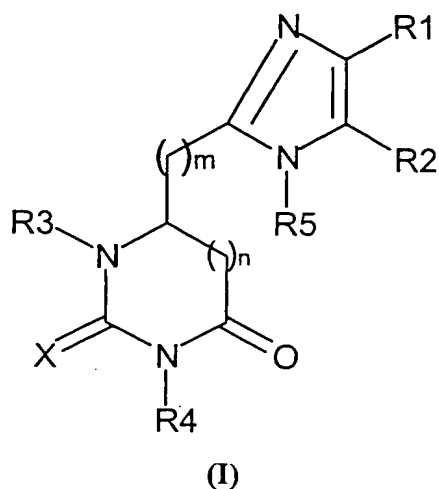
The invention relates to new derivatives of hydantoins, thiohydantoins, pyrimidinediones and thioxopyrimidinones of general formula (I) represented below, their preparation processes and their use as medicaments. These compounds have a good affinity with certain sub-types of somatostatin receptors and therefore have useful pharmacological properties. The invention also relates to the pharmaceutical compositions containing said compounds and their use for the preparation of a medicament intended to treat pathological states or diseases in which one (or more) somatostatin receptors are involved.

Somatostatin (SST) is a cyclic tetradecapeptide which was isolated for the first time from the hypothalamus as a substance which inhibits the growth hormone (Brazeau P. et al., *Science* 1973, **179**, 77-79). It also operates as a neurotransmitter in the brain (Reisine T. et al., *Neuroscience* 1995, **67**, 777-790; Reisine T. et al., *Endocrinology* 1995, **16**, 427-442). Molecular cloning has allowed it to be shown that the bioactivity of somatostatin depends directly on a family of five receptors linked to the membrane.

The heterogeneity of the biological functions of somatostatin has led to studies which try to identify the structure-activity relationships of peptide analogues on somatostatin receptors, which has led to the discovery of 5 sub-types of receptors (Yamada et al., *Proc. Natl. Acad. Sci. U.S.A.*, **89**, 251-255, 1992; Raynor, K. et al, *Mol. Pharmacol.*, **44**, 385-392, 1993). The functional roles of these receptors are currently being actively studied. The affinities with different sub-types of somatostatin receptors have been associated with the treatment of the following disorders/diseases. Activation of sub-types 2 and 5 has been associated with suppression of the growth hormone (GH) and more particularly with that of adenomas secreting GH (acromegalia) and those secreting hormone TSH. Activation of sub-type 2 but not sub-type 5 has been associated with the treatment of adenomas secreting prolactin. Other indications associated with the activation of sub-types of somatostatin receptors are the recurrence of stenosis, inhibition of the secretion of insulin and/or of glucagon and in particular diabetes mellitus, hyperlipidemia, insensibility to insulin, Syndrome X, angiopathy, proliferative

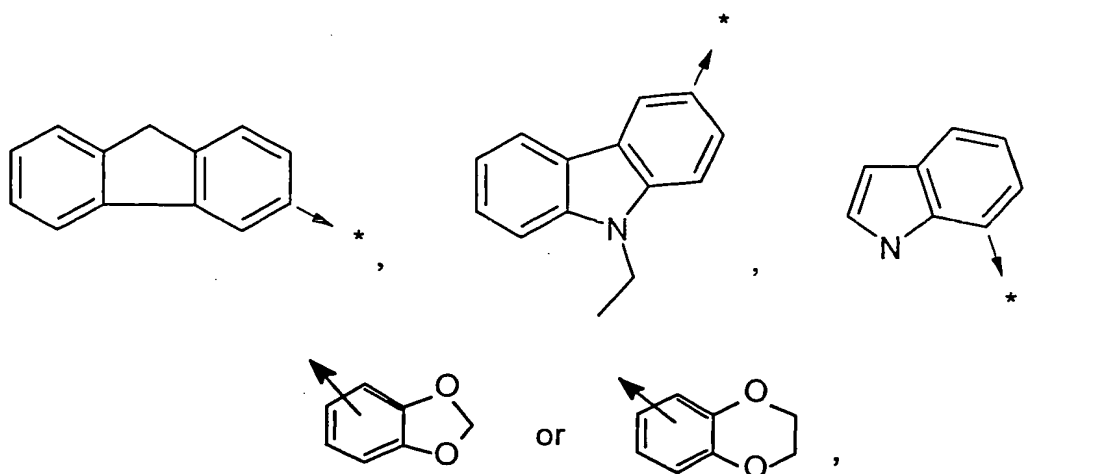
- retinopathy, dawn phenomenon and nephropathy; inhibition of the secretion of gastric acid and in particular peptic ulcers, enterocutaneous and pancreaticocutaneous fistulae, irritable colon syndrome, dumping syndrome, aqueous diarrhoea syndrome, diarrhoea associated with AIDS, diarrhoea induced by chemotherapy, acute or chronic
- 5 pancreatitis and secretory gastrointestinal tumours; the treatment of cancer such as hepatomas; the inhibition of angiogenesis, the treatment of inflammatory disorders such as arthritis; chronic rejection of allografts; angioplasty; the prevention of bleeding of grafted vessels and gastrointestinal bleeding. The agonists of somatostatin can also be used to reduce the weight of a patient.
- 10 Among the pathological disorders associated with somatostatin (Moreau J.P. et al., *Life Sciences* 1987, 40, 419; Harris A.G. et al., *The European Journal of Medicine*, 1993, 2, 97-105), there can be mentioned for example: acromegalia, hypophyseal adenomas, Cushing's disease, gonadotrophinomas and prolactinomas, catabolic side-effects of glucocorticoids, insulin dependent diabetes, diabetic retinopathy, diabetic nephropathy,
- 15 hyperthyroidism, gigantism, endocrinic gastroenteropancreatic tumours including carcinoid syndrome, VIPoma, insulinoma, nesidioblastoma, hyperinsulinemia, glucagonoma, gastrinoma and Zollinger-Ellison's syndrome, GRFoma as well as acute bleeding of the esophageal varices, gastroesophageal reflux, gastroduodenal reflux, pancreatitis, enterocutaneous and pancreatic fistulae but also diarrhoeas, refractory
- 20 diarrhoeas of acquired immunodeficiency syndrome, chronic secretory diarrhoea, diarrhoea associated with irritable bowel syndrome, disorders linked with gastrin releasing peptide, secondary pathologies with intestinal grafts, portal hypertension as well as haemorrhages of the varices in patients with cirrhosis, gastro-intestinal haemorrhage, haemorrhage of the gastroduodenal ulcer, Crohn's disease, systemic
- 25 scleroses, dumping syndrome, small intestine syndrome, hypotension, scleroderma and medullar thyroid carcinoma, illnesses linked with cell hyperproliferation such as cancers and more particularly breast cancer, prostate cancer, thyroid cancer as well as pancreatic cancer and colorectal cancer, fibroses and more particularly fibrosis of the kidney, fibrosis of the liver, fibrosis of the lung, fibrosis of the skin, also fibrosis of the
- 30 central nervous system as well as that of the nose and fibrosis induced by chemotherapy, and other therapeutic fields such as, for example, cephalas including cephalas associated with hypophyseal tumours, pain, panic attacks, chemotherapy, cicatrization of wounds, renal insufficiency resulting from delayed development, obesity and delayed development linked with obesity, delayed uterine development,
- 35 dysplasia of the skeleton, Noonan's syndrome, sleep apnea syndrome, Graves' disease, polycystic disease of the ovaries, pancreatic pseudocysts and ascites, leukaemia, meningioma, cancerous cachexia, inhibition of H pylori, psoriasis, as well as Alzheimer's disease. Osteoporosis can also be mentioned.

- The Applicant found that the compounds of general formula (I) described hereafter have an affinity and a selectivity for the somatostatin receptors. As somatostatin and its peptide analogues often have a poor bioavailability by oral route and a low selectivity (Robinson, C., *Drugs of the Future*, 1994, 19, 992; Reubi, J.C. et al., *TIPS*, 1995, 16, 110), said compounds, non-peptide agonists or antagonists of somatostatin, can be advantageously used to treat pathological states or illnesses as presented above and in which one (or more) somatostatin receptors are involved. Preferably, said compounds can be used for the treatment of acromegalia, hypophyseal adenomas or endocrine gastroenteropancreatic tumours including carcinoid syndrome.
- 10 The compounds of the present invention correspond to general formula (I)

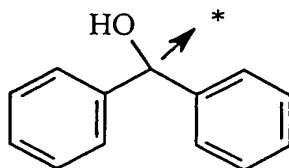


in racemic, enantiomeric form or all combinations of these forms, in which:

- R1 represents a (C_1-C_{12}) alkyl, (C_0-C_6) alkyl-C(O)-O-Z1, (C_0-C_6) alkyl-C(O)-NH-(CH₂)_p-Z2 or aryl radical optionally substituted,
- Z1 represents H, a (C_1-C_6) alkyl, -(CH₂)_p-aryl radical;
- 15 Z2 represents an amino, (C_1-C_{12}) alkylamino, (C_3-C_8) cycloalkylamino, N,N-di- (C_1-C_{12}) alkylamino, NH-C(O)-O-(CH₂)_p-phenyl, NH-C(O)-O-(CH₂)_p-(C₁-C₆)alkyl radical, an optionally substituted carbocyclic or heterocyclic aryl radical or an optionally substituted heterocyclic non aromatic radical;
- R2 represents H, (C_1-C_{12}) alkyl or aryl optionally substituted;
- 20 R3 represents H or (CH₂)_p-Z3;
- Z3 represents (C_1-C_{12}) alkyl, (C_1-C_{12}) alkenyl, (C_3-C_8) cycloalkyl, -Y1-(CH₂)_p-phenyl-(X1)_n, -S-(C₁-C₁₂)alkyl, S-(C₁-C₁₂)alkyl-S-S-(C₁-C₁₂)alkyl, an optionally substituted carbocyclic or heterocyclic aryl radical, and in particular one of the radicals represented below



an optionally substituted heterocyclic non aromatic radical, a *bis*-arylalkyl or di-arylalkyl radical or also the radical

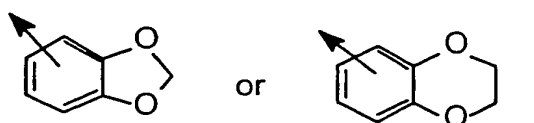


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Y1 represents O, S, NH or is absent;

R4 represents $(\text{CH}_2)_p\text{-Z4}$;

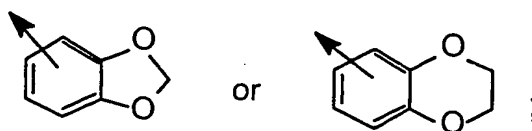
10 Z4 represents amino, $(\text{C}_1\text{-C}_{12})$ alkyl, $(\text{C}_3\text{-C}_8)$ cycloalkyl, $(\text{C}_1\text{-C}_{12})$ alkylamino, N,N-di- $(\text{C}_1\text{-C}_{12})$ alkylamino, amino $(\text{C}_3\text{-C}_6)$ cycloalkyl, amino $(\text{C}_1\text{-C}_6)$ alkyl $(\text{C}_3\text{-C}_6)$ cycloalkyl $(\text{C}_1\text{-C}_6)$ alkyl, carbocyclic or heterocyclic aminoaryl, $(\text{C}_1\text{-C}_{12})$ alkoxy, $(\text{C}_1\text{-C}_{12})$ alkenyl, N-C(O)O $(\text{C}_1\text{-C}_6)$ alkyl, an optionally substituted carbocyclic or heterocyclic aryl radical, an optionally substituted heterocyclic non aromatic radical, *bis*-arylalkyl, di-arylalkyl or one of the radicals represented below



15 or also Z4 represents an N(R6)(R7) radical in which R6 and R7 taken together with the nitrogen atom which they carry form together a heterocycle with 5 to 7 members;

R5 represents H, $-(\text{CH}_2)_p\text{-C(O)-}(\text{CH}_2)_p\text{-Z5}$, $-(\text{CH}_2)_p\text{-Z5}$, $-(\text{CH}_2)_p\text{-OZ5}$ or $-(\text{C}_0\text{-C}_6)$ alkyl-C(O)-NH- $(\text{CH}_2)_p\text{-Z5}$,

Z5 representing an optionally substituted radical chosen from the group constituted by the $-(C_1-C_{12})$ alkyl, benzo[b]thiophene, phenyl, naphthyl, benzo[b]furannyl, thiophene, isoxazolyl, indolyl radicals, and



- 5 it being understood that an optionally substituted radical or an optionally substituted phenyl is optionally substituted by one or more substituent, each preferably chosen independently from the group constituted by the Cl, F, Br, I, CF_3 , NO_2 , OH, NH_2 , CN, N_3 , $-OCF_3$, (C_1-C_{12}) alkyl, (C_1-C_{12}) alkoxy, $-(CH_2)_p$ -phenyl- $(X1)_q$, $-NH-CO-(C_1-C_6)$ alkyl, $-NH-C(O)O-(C_1-C_6)$ alkyl, $-S-(C_1-C_6)$ alkyl, $-S$ -phenyl- $(X1)_q$, $-O-(CH_2)_p$ -phenyl- $(X1)_q$, $-(CH_2)_p-C(O)-O-(C_1-C_6)$ alkyl, $-(CH_2)_p-C(O)-(C_1-C_6)$ alkyl, $-O-(CH_2)_p-NH_2$, $-O-(CH_2)_p-NH-(C_1-C_6)$ alkyl, $-O-(CH_2)_p-N$ -di- $((C_1-C_6)$ alkyl) and $-((C_0-C_{12}))$ alkyl- $(X1)_q$ radicals;

- X1, each time that it occurs, is independently chosen from the group constituted by the H, Cl, F, Br, I, CF_3 , NO_2 , OH, NH_2 , CN, N_3 , $-OCF_3$, (C_1-C_{12}) alkyl, (C_1-C_{12}) alkoxy, $-S-(C_1-C_6)$ alkyl, $-(CH_2)_p$ -amino, $-(CH_2)_p-NH-(C_1-C_6)$ alkyl, $-(CH_2)_p-N$ -di- $((C_1-C_6)$ alkyl), $-(CH_2)_p$ -phenyl and $-(CH_2)_p-NH-(C_3-C_6)$ cycloalkyl radicals;

p each time that it occurs is independently 0 or an integer from 1 to 6;

q each time that it occurs is independently an integer from 1 to 5.

X represents O or S;

n represents 0 or 1; and finally

- 20 when n represents 0, m represents 1, 2 or 3, and when n represents 1, m represents 0 or 1.

According to a preferred variant of the invention, the compounds of general formula (I) are such that R5 represents H.

- 25 The compounds of general formula (I) can, if appropriate, contain more than one asymmetrical centre. If this happens, the diastereomers or any mixture of diastereomers are also included in the invention. For example, when the compound of general formula (I) has two asymmetrical centres, the invention will include the compounds of general formula (I) of "R,S", "S,R", "R,R" and "S,S" configurations, as well as a mixture in whatever proportions of the latter.

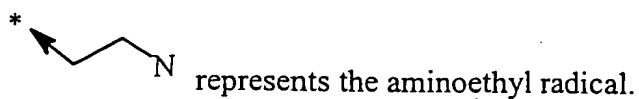
In the present invention, the alkyl radicals can be linear or branched. By alkyl, unless specified otherwise, is meant a linear or branched alkyl radical containing 1 to 6 carbon atoms. By cycloalkyl, unless specified otherwise, is meant a monocyclic carbon system containing 3 to 7 carbon atoms. By alkenyl, unless specified otherwise, is meant a linear or branched alkyl radical containing 1 to 6 carbon atoms and having at least one unsaturation (double bond). By alkynyl, unless specified otherwise, is meant a linear or branched alkyl radical containing 1 to 6 carbon atoms and having at least one double unsaturation (triple bond). By carbocyclic or heterocyclic aryl, is meant a carbocyclic or heterocyclic system containing at least one aromatic ring, a system being called heterocyclic when at least one of the rings which comprise it contains a heteroatom (O, N or S). By aryl, unless specified otherwise, is meant a carbocyclic system comprising at least one aromatic ring. By haloalkyl, is meant an alkyl radical of which at least one of the hydrogen atoms (and optionally all) is replaced by a halogen atom. By heterocyclic non aromatic radical, is meant a heterocyclic system containing no aromatic ring, at least one of the rings comprising said system containing at least one heteroatom (O, N or S).

By alkylthio, alkoxy, haloalkyl, haloalkoxy, aminoalkyl, alkylamino, alkenyl, alkynyl and aralkyl radicals, is meant respectively the alkylthio, alkoxy, haloalkyl, haloalkoxy, aminoalkyl, alkylmino, alkenyl, alkynyl and aralkyl radicals the alkyl radical of which has the meaning indicated previously.

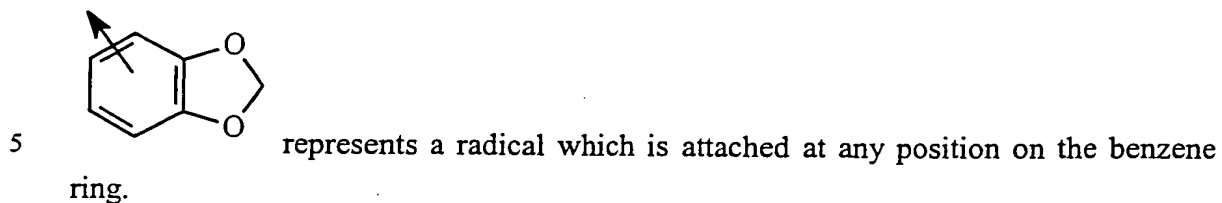
By N,N-di-(C₁-C₁₂)alkylamino radical, is meant a dialkylamino radical of which the two alkyl radicals substituting the nitrogen atom can have independently 1 to 12 carbon atoms.

By linear or branched alkyl having 1 to 6 carbon atoms, is meant in particular the methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl and tert-butyl, pentyl, neopentyl, isopentyl, hexyl, isohexyl radicals. By cycloalkyl, is meant in particular the cyclopropanyl, cyclobutanyl, cyclopentanyl, cyclohexyl and cycloheptanyl radicals. By carbocyclic or heterocyclic aryl, is meant in particular the phenyl, naphthyl, pyridinyl, furannyl, pyrrolyl, thiophenyl, thiazolyl, indanyl, indolyl, imidazolyl, benzofurannyl, benzothiophenyl, phthalimidyl radicals. By carbocyclic or heterocyclic aralkyl, is meant in particular the benzyl, phenylethyl, phenylpropyl, phenylbutyl, indolylalkyl, phthalimidoalkyl radicals.

When an arrow emanates from a chemical structure, said arrow indicates the attachment point. For example:



When an arrow is drawn through a bi- or tricyclic group, said arrow indicates that said bi- or tricyclic group can be attached by any of the available attachment points on any aromatic ring of said group. For example:

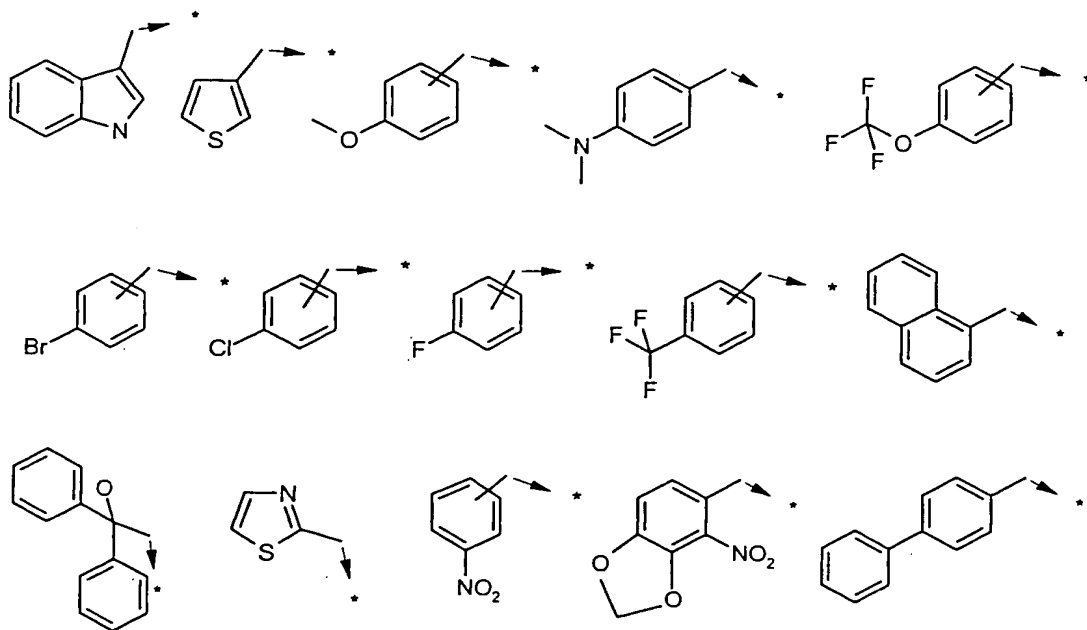


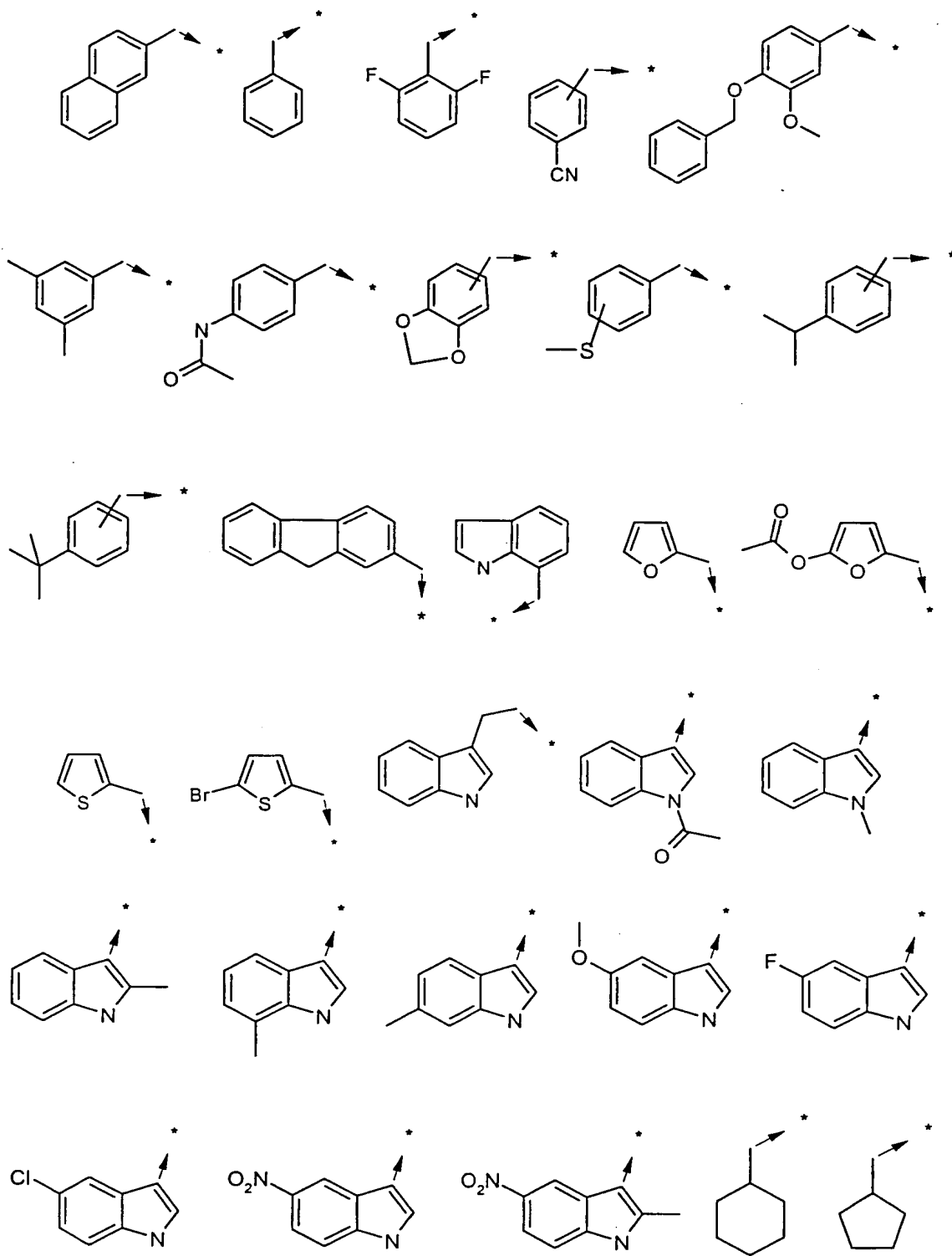
In particular, the compounds of general formula (I) according to the invention can be chosen such that:

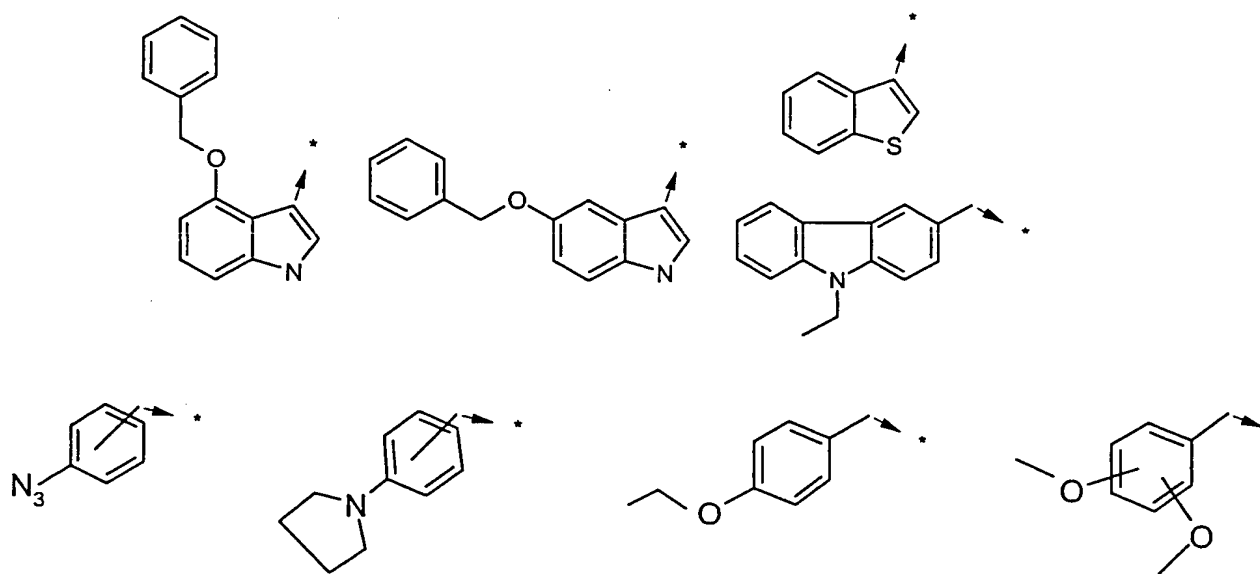
R1 represents an optionally substituted aryl radical;

10 R2 represents H or an alkyl radical;

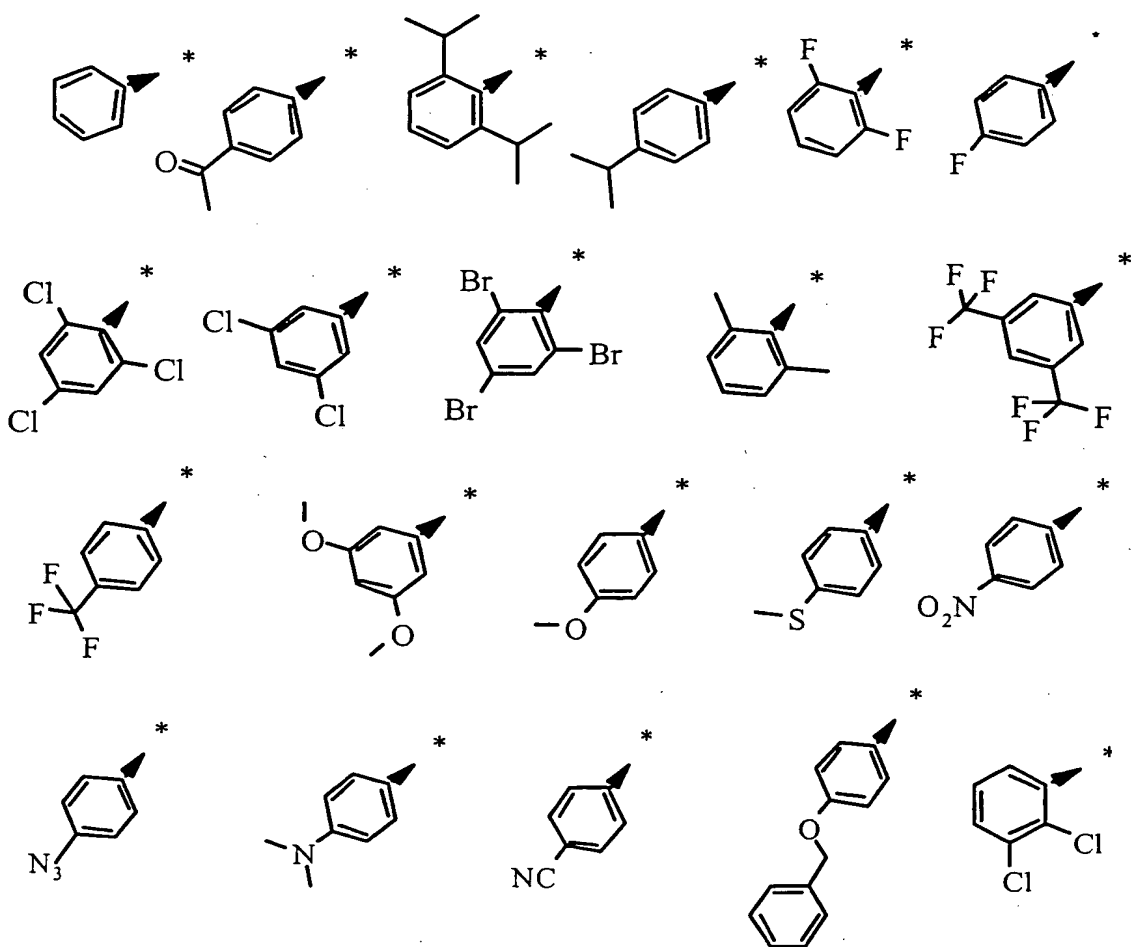
R3 represents one of the following radicals:

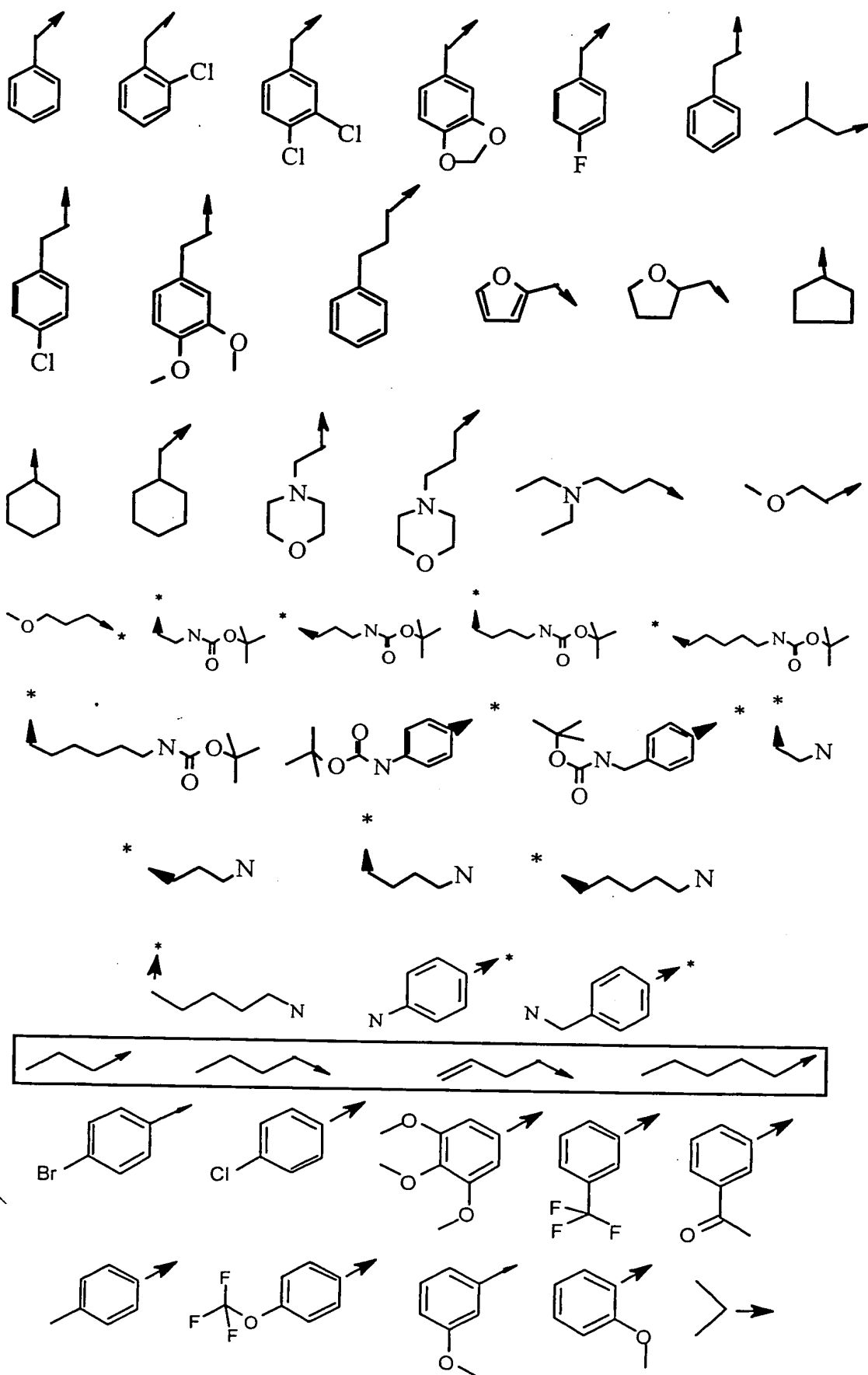


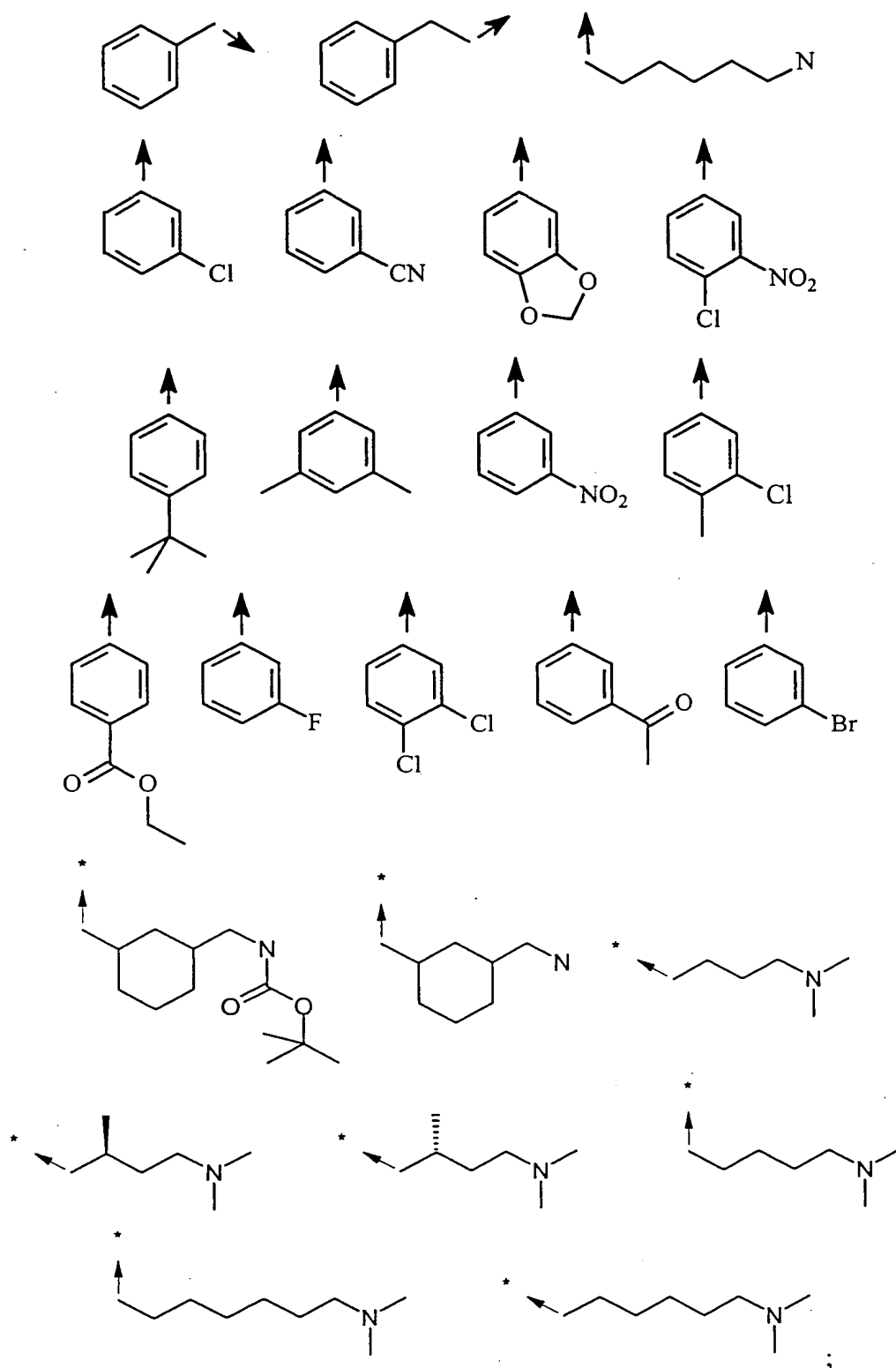




R4 represents one of the following radicals:







R5 represents H or an alkyl radical.

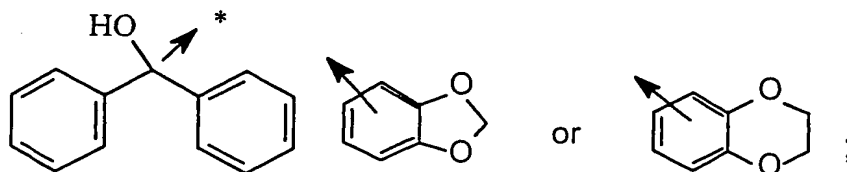
Preferably, the compounds of general formula (I) are such that:

R1 represents the phenyl radical optionally substituted by a halogen atom or a (C₁-C₁₂)alkyl, (C₁-C₁₂)alkoxy or nitro radical;

R2 and R5 represent H or alkyl;

R3 represents H or (CH₂)_p-Z3;

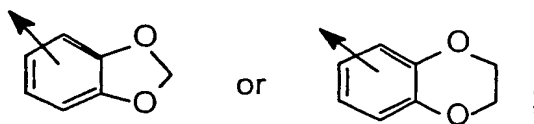
- 5 Z3 represents (C₁-C₁₂)alkyl, (C₃-C₈)cycloalkyl, Y1-(CH₂)_p-phenyl-(X1)_n, an optionally substituted carbocyclic or heterocyclic aryl radical, an optionally substituted heterocyclic non aromatic radical, *bis*-arylalkyl, di-arylalkyl or one of the radicals represented below



- 10 Y1 represents O, S, NH or is absent;

R4 represents (CH₂)_p-Z4;

- Z4 represents amino, (C₃-C₈)cycloalkyl, (C₁-C₁₂)alkylamino, N,N-di-(C₁-C₁₂)alkylamino, amino(C₃-C₈)cycloalkyl, amino(C₁-C₆)alkyl(C₃-C₈)cycloalkyl(C₁-C₆)alkyl, carbocyclic or heterocyclic aminoaryl, an optionally substituted carbocyclic or
 15 heterocyclic aryl radical, an optionally substituted heterocyclic non aromatic radical, *bis*-arylalkyl, di-arylalkyl or one of the radicals represented below



- it being understood that an optionally substituted radical or an optionally substituted phenyl is optionally substituted by one or more substituent, each preferably chosen
 20 independently from the group constituted by the Cl, F, Br, I, CF₃, NO₂, OH, NH₂, CN, N₃, -OCF₃, (C₁-C₁₂)alkyl, (C₁-C₁₂)alkoxy, -(CH₂)_p-phenyl-(X1)_q, -NH-CO-(C₁-C₆)alkyl, -NH-C(O)O-(C₁-C₆)alkyl, -S-(C₁-C₆)alkyl, -S-phenyl-(X1)_q, -O-(CH₂)_p-phenyl-(X1)_q, -(CH₂)_p-C(O)-O-(C₁-C₆)alkyl, -(CH₂)_p-C(O)-(C₁-C₆)alkyl, -O-(CH₂)_p-NH₂, -O-(CH₂)_p-NH-(C₁-C₆)alkyl, -O-(CH₂)_p-N-di-((C₁-C₆)alkyl) and -((C₀-C₁₂))alkyl-(X1)_q radicals;
 25 X1, each time that it occurs, is independently chosen from the group constituted by the H, Cl, F, Br, I, CF₃, NO₂, OH, NH₂, CN, N₃, -OCF₃, (C₁-C₁₂)alkyl, (C₁-C₁₂)alkoxy, -S-(C₁-C₆)alkyl, -(CH₂)_p-amino, -(CH₂)_p-NH-(C₁-C₆)alkyl, -(CH₂)_p-N-di-((C₁-C₆)alkyl), -(CH₂)_p-phenyl and -(CH₂)_p-NH-(C₃-C₈)cycloalkyl radicals;

p each time that it occurs is independently 0 or an integer from 1 to 6;

q each time that it occurs is independently an integer from 1 to 5.

X represents O or S;

n represents 0 or 1; and finally

- 5 when n represents 0, m represents 1, 2 or 3, and when n represents 1, m represents 0 or 1.

More preferentially, the compounds of general formula (I) are such that:

R1 represents the phenyl radical optionally substituted by a halogen atom or a (C₁-C₁₂)alkyl, (C₁-C₁₂)alkoxy or nitro radical;

- 10 R2 and R5 represent H or alkyl;

R3 represents (CH₂)_p-Z3,

Z3 representing a (C₃-C₈)cycloalkyl radical or an optionally substituted radical chosen from the phenyl, naphthyl, furannyl, thiophene, indolyl, pyrrolyl and benzothiophene radicals;

- 15 R4 represents (CH₂)_p-Z4;

Z4 representing amino, (C₁-C₁₂)alkylamino, N,N-di-(C₁-C₁₂)alkylamino or amino(C₁-C₆)alkyl(C₃-C₆)cycloalkyl-(C₁-C₆)alkyl;

X represents S;

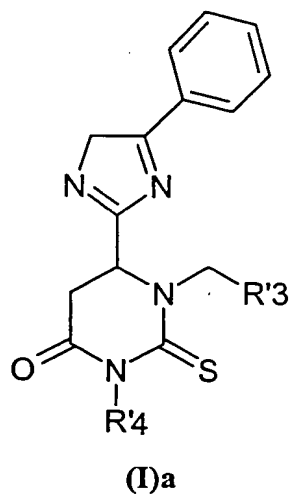
p each time that it occurs is independently 0 or an integer from 1 to 6;

- 20 m represents 0, 1 or 2; and finally

n represents 0 or 1.

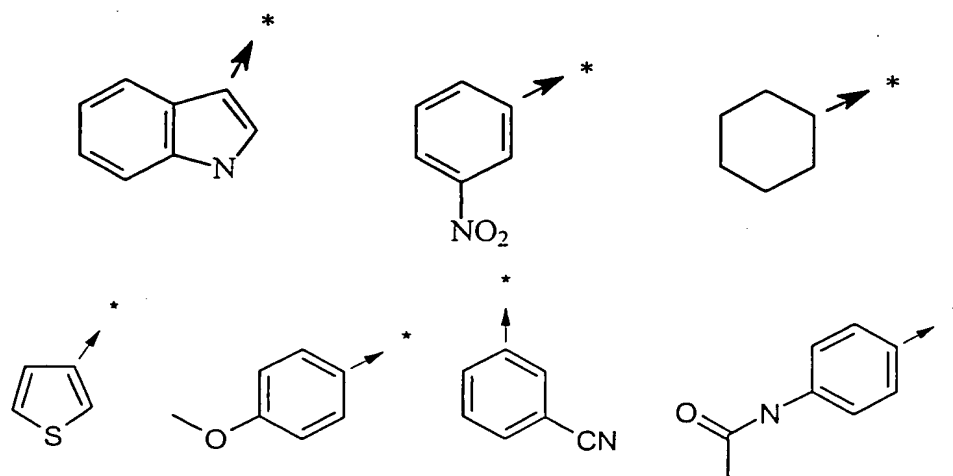
Yet more preferentially, the compounds of the present invention are of the compounds:

- of general sub-formula (I)**a** represented below:

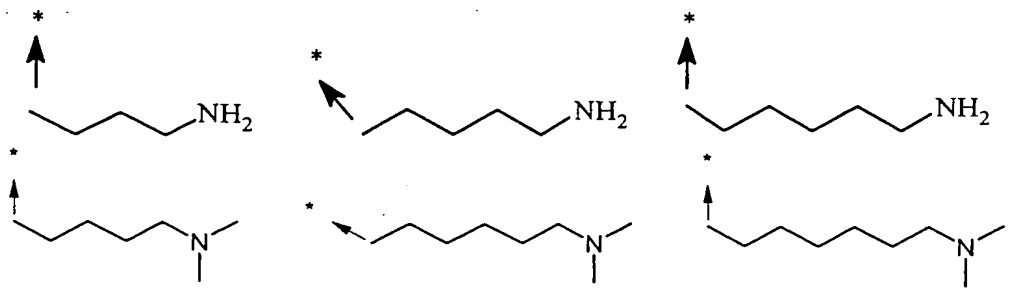


in which:

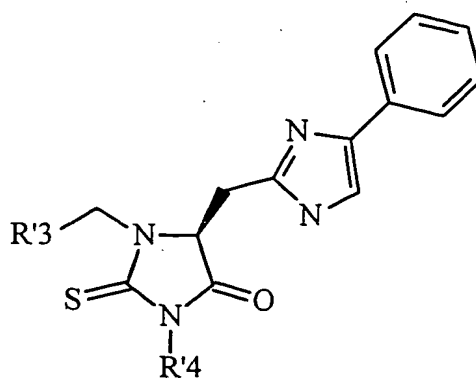
R'3 represents one of the radicals represented below:



and R'4 represents one of the radicals represented below:



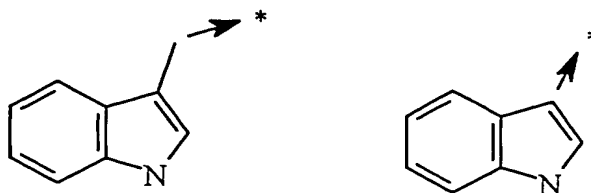
- of general sub-formula **(I)b** represented below:



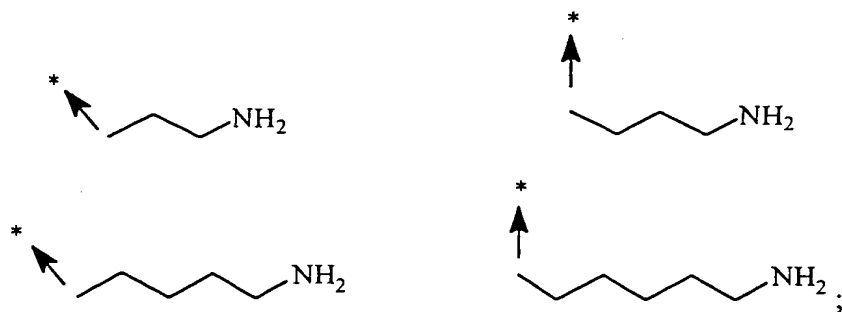
(Ib)

in which:

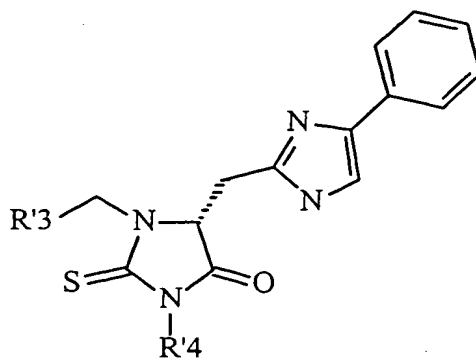
R'3 represents one of the radicals represented below:



and R'4 represents one of the radicals represented below:



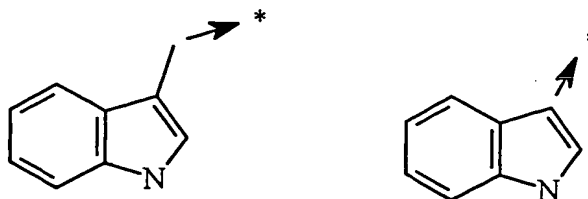
- of general sub-formula (Ic) represented below:



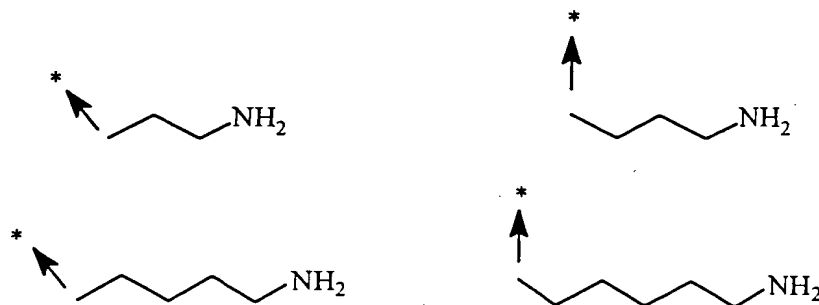
(Ic)

in which:

R'3 represents one of the radicals represented below:

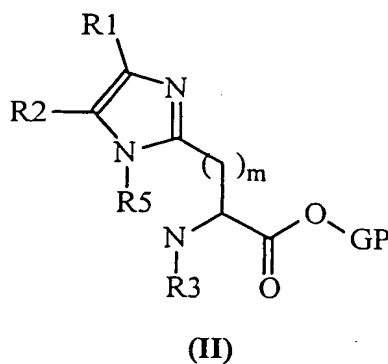


and R'4 represents one of the radicals represented below:



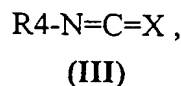
The invention relates moreover to the preparation processes for the compounds of
5 general formula (I) described previously (also applicable to the corresponding
compounds of general sub-formulae (I)a, (I)b and (I)c).

The compounds of general formula (I) described previously for which n represents 0
and X represents O or S can be prepared by the reaction in an aprotic solvent of the
compound of general formula (II) represented below



10 in which m, R1, R2, R3 and R5 have the same meaning as in general formula (I), and
the O-GP radical is a parting protective group derived from an alcohol and in particular
benzyloxy, methoxy or tert-butoxy,

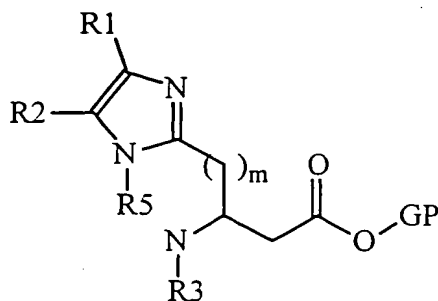
with an isocyanate or isothiocyanate of general formula (III)



in which R4 and X have the same meaning as in general formula (I),

preferably in the presence of a tertiary base for a duration of approximately 1 to 24 hours and at a temperature preferably comprised between 20 and 60 °C.

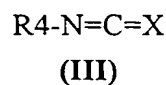
The compounds of general formula (I) described previously for which n represents 1 and X represents O or S can be prepared by the reaction in an aprotic solvent of the compound of general formula (IV) represented below



(IV)

in which m, R1, R2, R3 and R5 have the same meaning as in general formula (I), and the O-GP radical is a parting protective group derived from an alcohol and in particular benzyloxy, methoxy or tert-butoxy,

with an isocyanate or isothiocyanate of general formula (III)

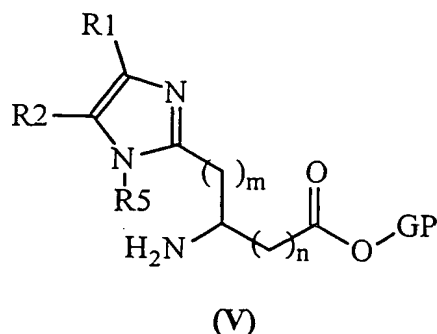


in which R4 and X have the same meaning as in general formula (I),

preferably in the presence of a tertiary base for a duration of approximately 1 to 48 hours and at a temperature preferably comprised between 20 and 70 °C.

For the above processes, the aprotic solvent is preferably polar and can in particular be THF or dichloromethane. The tertiary base will be for example triethylamine or *N,N*-diisopropylethylamine.

Moreover the invention offers new synthesis intermediates which are useful for the preparation of the compounds of general formula (I). These compounds, precursors of the compounds of general formula (II) and (IV), correspond to general formula (V):



in which

R1, R2, R5, m and n have the same meaning as in general formula (I);

and the O-GP radical is a parting protective group derived from an alcohol and in particular benzyloxy, methoxy or tert-butoxy.

5 The following compounds corresponding to general formula (V) are the preferred intermediates:

- benzyl (2*S*)-2-amino-3-[(4-phenyl)-1*H*-imidazol-2-yl]propanoate;

- benzyl (2*R*)-2-amino-3-[(4-phenyl)-1*H*-imidazol-2-yl]propanoate;

- benzyl (2*S*)-2-amino-4-[(4-phenyl)-1*H*-imidazol-2-yl]butanoate;

10 - benzyl (2*R*)-2-amino-4-[(4-phenyl)-1*H*-imidazol-2-yl]butanoate;

- benzyl (3*R*)-3-amino-4-[(4-phenyl)-1*H*-imidazol-2-yl]propanoate;

- benzyl (3*S*)-3-amino-4-[(4-phenyl)-1*H*-imidazol-2-yl]propanoate .

A subject of the invention is also, as medicaments, the compounds of general formulae (I), (I)a, (I)b and (I)c described previously or their pharmaceutically acceptable salts.

15 It also relates to the pharmaceutical compositions containing said compounds or their pharmaceutically acceptable salts, and their use for the preparation of a medicament intended to treat the pathological states or diseases in which one (or more) of the somatostatin receptors are involved.

20 In particular, the compounds of general formulae (I), (I)a, (I)b and (I)c described previously or their pharmaceutically acceptable salts can be used for the preparation of a medicament intended to treat the pathological states or diseases chosen from the group comprising the following pathological states or diseases: acromegalia, hypophyseal adenomas, Cushing's disease, gonadotrophinomas and prolactinomas,

catabolic side-effects of glucocorticoids, insulin dependent diabetes, diabetic retinopathy, diabetic nephropathy, syndrome X, dawn phenomena, angiopathy, angioplasty, hyperthyroidism, gigantism, endocrinic gastroenteropancreatic tumours including carcinoid syndrome, VIPoma, insulinoma, nesidioblastoma, 5 hyperinsulinemia, glucagonoma, gastrinoma and Zollinger-Ellison's syndrome, GRFoma as well as acute bleeding of the esophageal varices, ulcers, gastroesophageal reflux, gastroduodenal reflux, pancreatitis, enterocutaneous and pancreatic fistulae but also diarrhoeas, refractory diarrhoeas of acquired immunodeficiency syndrome, chronic secretory diarrhoea, diarrhoea associated with irritable bowel syndrome, diarrhoeas 10 induced by chemotherapy, disorders linked with gastrin releasing peptide, secondary pathologies with intestinal grafts, portal hypertension as well as haemorrhages of the varices in patients with cirrhosis, gastro-intestinal haemorrhage, haemorrhage of the gastroduodenal ulcer, bleeding of grafted vessels, Crohn's disease, systemic scleroses, dumping syndrome, small intestine syndrome, hypotension, scleroderma and medullar 15 thyroid carcinoma, illnesses linked with cell hyperproliferation such as cancers and more particularly breast cancer, prostate cancer, thyroid cancer as well as pancreatic cancer and colorectal cancer, fibroses and more particularly fibrosis of the kidney, fibrosis of the liver, fibrosis of the lung, fibrosis of the skin, also fibrosis of the central nervous system as well as that of the nose and fibrosis induced by chemotherapy, and in 20 other therapeutic fields, cephalaeas including cephalaea associated with hypophyseal tumours, pain, inflammatory disorders such as arthritis, panic attacks, chemotherapy, cicatrization of wounds, renal insufficiency resulting from delayed development, hyperlipidemia, obesity and delayed development linked with obesity, delayed uterine development, dysplasia of the skeleton, Noonan's syndrome, sleep apnea syndrome, 25 Graves' disease, polycystic disease of the ovaries, pancreatic pseudocysts and ascites, leukaemia, meningioma, cancerous cachexia, inhibition of H pylori, psoriasis, chronic rejection of allografts as well as Alzheimer's disease and finally osteoporosis.

Preferably, the compounds of general formulae (I), (I)a, (I)b and (I)c described previously or their pharmaceutically acceptable salts can be used for the preparation of 30 a medicament intended to treat the pathological states or diseases chosen from the group comprising the following pathological states or diseases: acromegalia, hypophyseal adenomas or endocrinic gastroenteropancreatic tumours including carcinoid syndrome, and gastrointestinal bleeding.

By pharmaceutically acceptable salt is meant in particular addition salts of inorganic 35 acids such as hydrochloride, sulphate, phosphate, diphosphate, hydrobromide and nitrate, or of organic acids, such as acetate, maleate, fumarate, tartarate, succinate, citrate, lactate, methanesulphonate, p-toluenesulphonate, pamoate, oxalate and stearate.

The salts formed from bases such as sodium or potassium hydroxide also fall within the scope of the present invention, when they can be used. For other examples of pharmaceutically acceptable salts, reference can be made to "Pharmaceutical salts", *J. Pharm. Sci.* 66:1 (1977).

- 5 The pharmaceutical composition can be in the form of a solid, for example powders, granules, tablets, capsules, liposomes or suppositories. Appropriate solid supports can be for example calcium phosphate, magnesium stearate, talc, sugars, lactose, dextrin, starch, gelatin, cellulose, methyl cellulose, sodium carboxymethyl cellulose, polyvinylpyrrolidone and wax.
- 10 The pharmaceutical compositions containing a compound of the invention can also be presented in the form of a liquid, for example, solutions, emulsions, suspensions or syrups. Appropriate liquid supports can be, for example, water, organic solvents such as glycerol or the glycols, as well as their mixtures, in varying proportions, in water. The suspensions contain in particular suspensions of sustained release microparticles
- 15 loaded with active ingredient (in particular microparticles of polylactide-co-glycolide or PLGA - cf. for example the Patents US 3,773,919, EP 52 510 or EP 58 481 or the Patent Application PCT WO 98/47489), which allow the administration of a determined daily dose over a period of several days to several weeks.

20 The administration of a medicament according to the invention can be done by topical, oral, parenteral route, by intramuscular injection, etc.

The administration dose envisaged for a medicament according to the invention is comprised between 0.1 mg to 10 g according to the type of active compound used.

These compounds are prepared according to the following procedures.

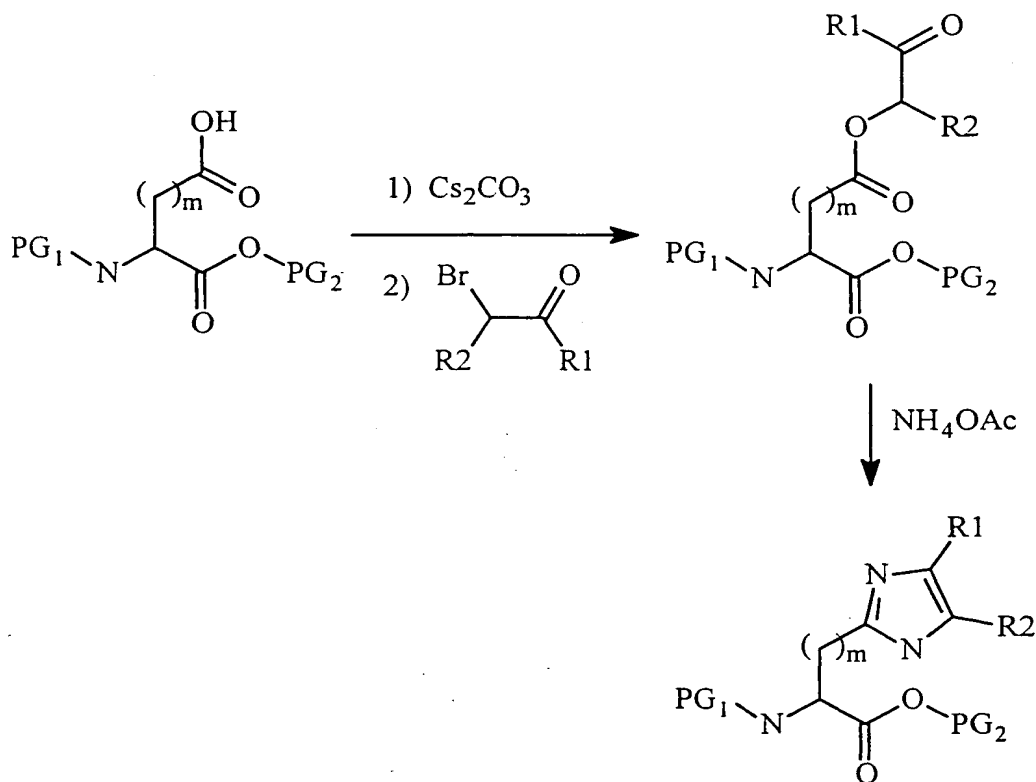
PREPARATION OF THE COMPOUNDS OF THE INVENTION

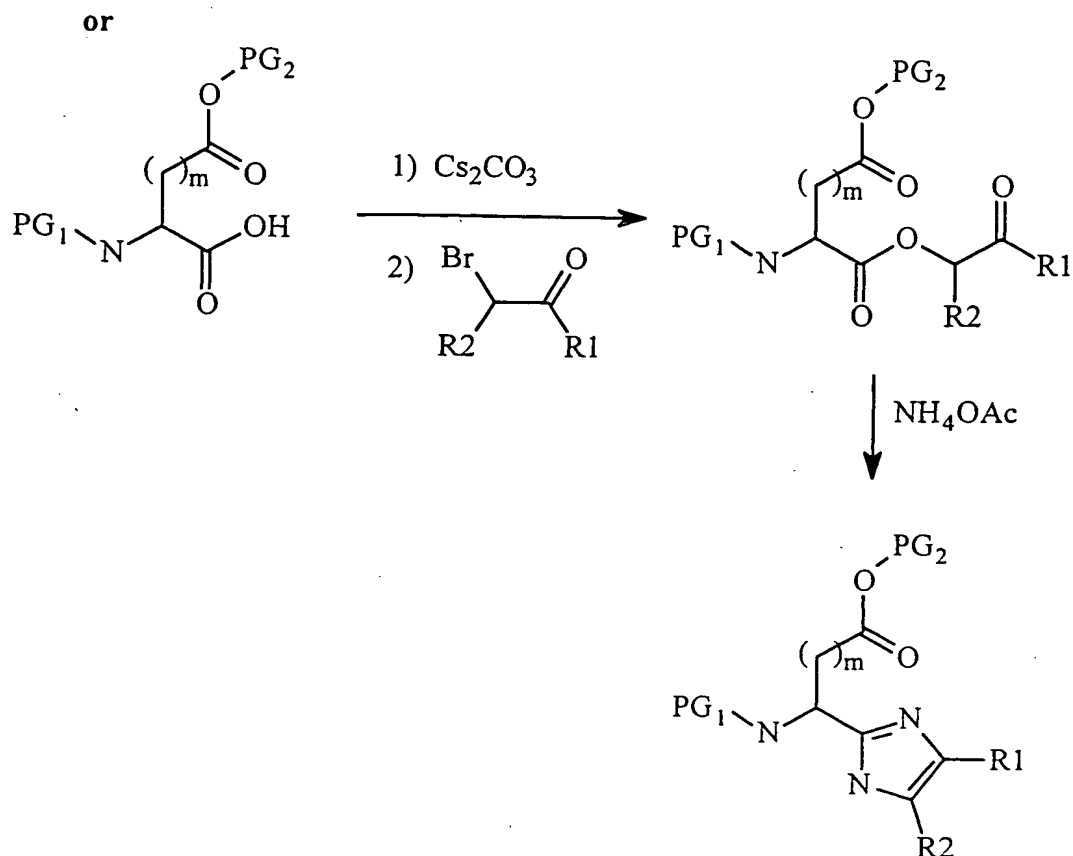
PREPARATION OF IMIDAZOLYL DERIVATIVES

General procedure:

i) Cyclization in order to obtain the imidazole group:

An amino acid is converted to its cesium salt using cesium carbonate in a polar solvent such as a DMF/H₂O (1:1) or EtOH/H₂O (1:1) mixture. An ester is then obtained using an appropriate bromoketone in an aprotic polar solvent such as anhydrous DMF. The cesium bromide formed is eliminated by filtration and ammonium acetate is added in an aprotic solvent having a high boiling temperature such as xylene or toluene or in an acidic aprotic solvent such as acetic acid. The mixture is maintained under reflux using a Dean-Stark trap for 30 minutes to one hour. In the diagram directly below, PG1 is a protective group, preferably a carbamate, such as t-Boc or benzylcarbamate, and PG2 is also a protective group, preferably a benzyl group.



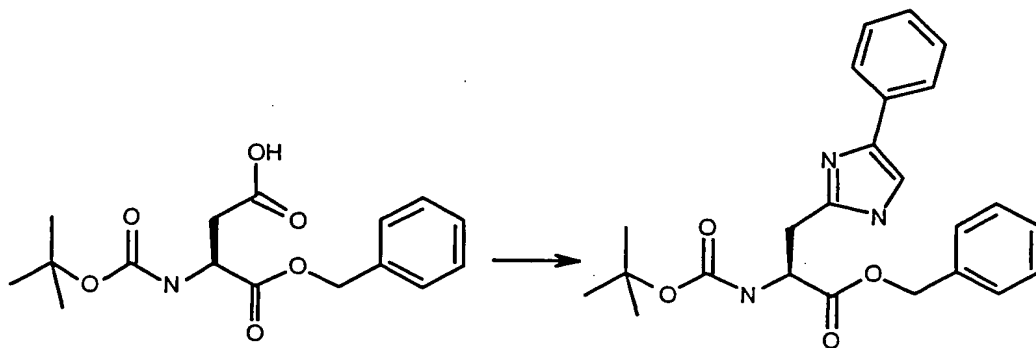


ii) *N*-substitution on the imidazole group:

If appropriate, the N-substitution on the imidazole group is carried out by the reaction described hereafter for the compounds of general formula (I) for which R5 does not represent H.

- 5 A solution of the intermediate obtained in the preceding stage, an alkylating agent such as an -bromoketone, an -bromoester, an alkyl or aryl bromide, is heated to a temperature of 20 to 80 °C for a duration of 2 to 48 hours in the presence of an organic or inorganic base (optionally supported on a resin such as polystyrene resin), in an aprotic solvent such as THF, acetonitrile or DMF.

Preparation of benzyl (2S)-2-[(tert-butoxycarbonyl)amino]-3-(4-phenyl-1H-imidazol-2-yl)propanoate



5

A solution of Boc-L-Asp-OBn (12 g; 37.1 mmol) and cesium carbonate (6.05 g; 0.5 eq.) is stirred for approximately 30 minutes at approximately 20°C in EtOH/H₂O (1:1, 7 ml), then concentrated under reduced pressure at approximately 40°C.

- 10 25 ml of a solution of 2-bromoacetophenone (7.38 g; 1 eq.) in dry DMF is added to the resulting salt dissolved in 130 ml of dry DMF. The mixture is stirred for approximately 1 hour at approximately 20°C under an argon atmosphere then concentrated under reduced pressure. Ethyl acetate is added (100 ml) and the mixture filtered, CsBr being washed with ethyl acetate. The filtrate is then concentrated under reduced pressure.

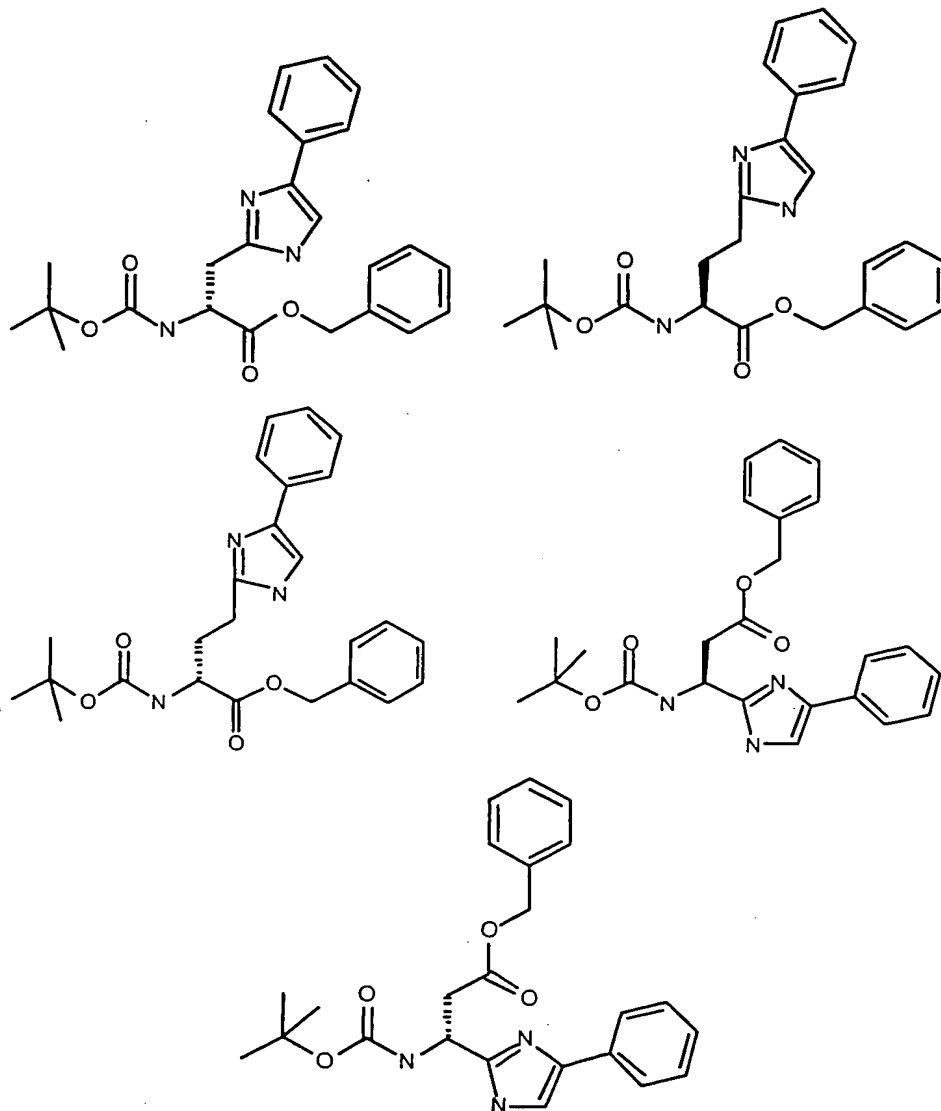
- 15 A solution of the residue obtained and ammonium acetate (58 g; 20 eq.) in xylene (280 ml) is maintained under reflux for approximately 30 minutes at approximately 140°C. The excess NH₄OAc and water are eliminated using a Dean-Stark trap. The progress of the reaction is monitored by thin layer chromatography (TLC; eluent: ethyl acetate / heptane 1:1). The mixture is then taken to approximately 20°C then washed successively with water, a saturated solution of NaHCO₃ solution until a basic pH is
20 obtained then with salt water until a neutral pH is obtained. The organic phase is then dried over Na₂SO₄ and concentrated under reduced pressure.

Purification of the resulting residue by flash chromatography on silica gel (eluent: ethyl acetate / heptane 1:1) yields the expected compound (8.2 g; 52 %).

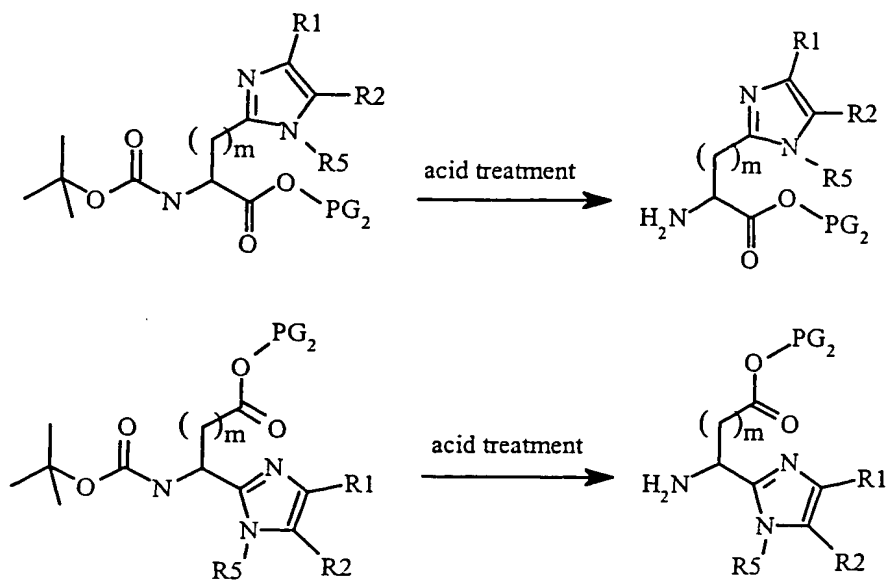
- 25 NMR (¹H, 400 MHz, CDCl₃): 7.64-7.14 (m, 11H, arom H); 5.95 (d, 1H, NHBoc); 5.21-5.13 (AB, 2H, OCH₂Ph, J_{AB} = 12Hz); 4.73 (m, 1H, CH); 3.30 (m, 2H, CH₂); 1.42 (s, 9H, (CH₃)₃C).

MS/LC: calculated MM = 421.2; m/z = 422.2 (M+H).

The following compounds are prepared in an analogous fashion to the procedure described for benzyl (2S)-2-[(tert-butoxycarbonyl)amino]-3-(4-phenyl-1H-imidazol-2-yl)propanoate:

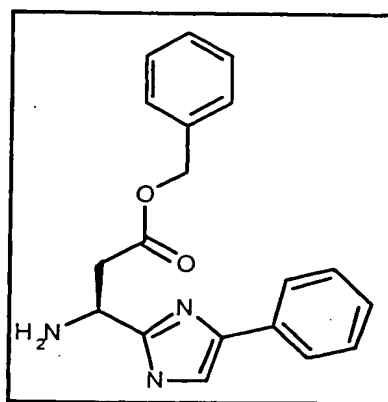


Deprotection stage



General procedure: the imidazolyl derivatives protected by N-Boc are treated with an organic or inorganic acid such as trifluoroacetic acid or hydrogen chloride (aqueous or in gaseous form) in an aprotic solvent such as dichloromethane or ethyl acetate at a temperature comprised between 0°C and 25°C for 0.5 to 5 hours.

Preparation of the dihydrochloride of benzyl (3S)-3-(4-phenyl-1H-imidazol-2-yl)-3-amino-propanoate



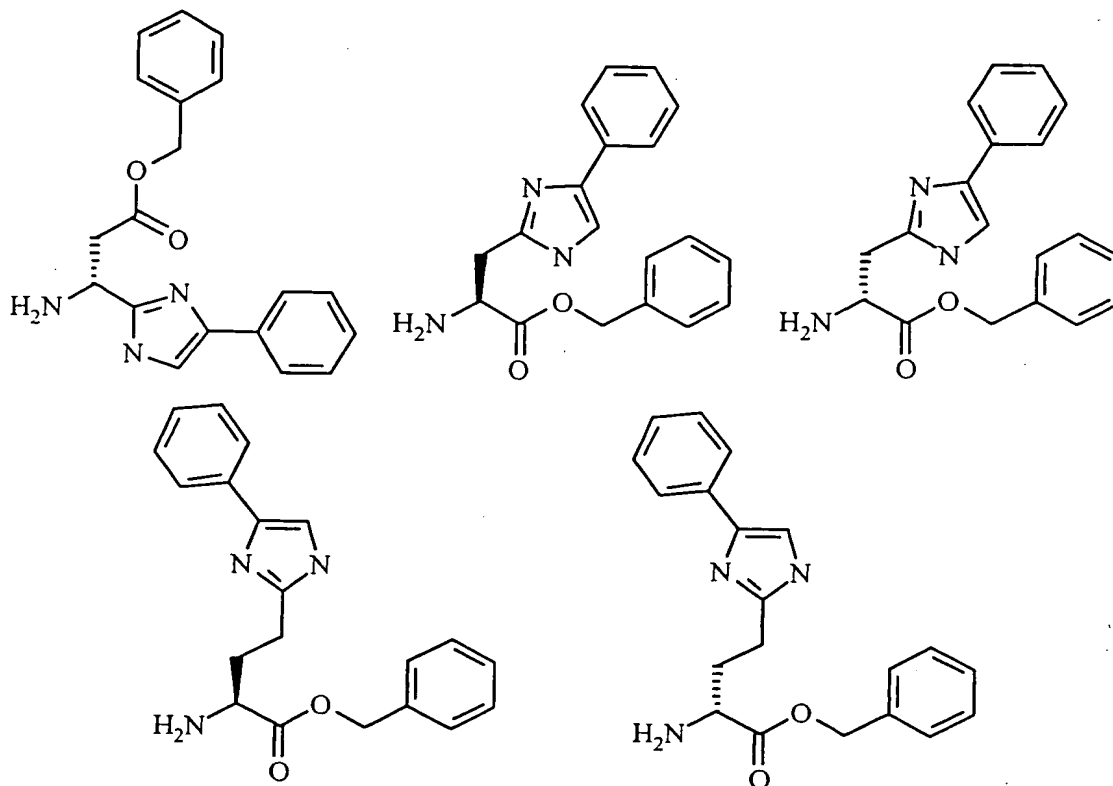
A flow of dry HCl is passed through a solution of benzyl (3S)-3-(4-phenyl-1H-imidazol-2-yl)-3-[(tert-butoxycarbonyl)amino]propanoate (5 g) in ethyl acetate (120 ml) at 0°C until the TLC (eluent: 100% ethyl acetate) shows that the starting compound has

completely disappeared. The resulting mixture is then evaporated under reduced pressure. Diethylether is added to the solid obtained and the mixture is filtered. The hydrochloride is washed several times with dichloromethane then diethylether and dried under reduced pressure to produce 4.6 g of expected compound (98 % yield).

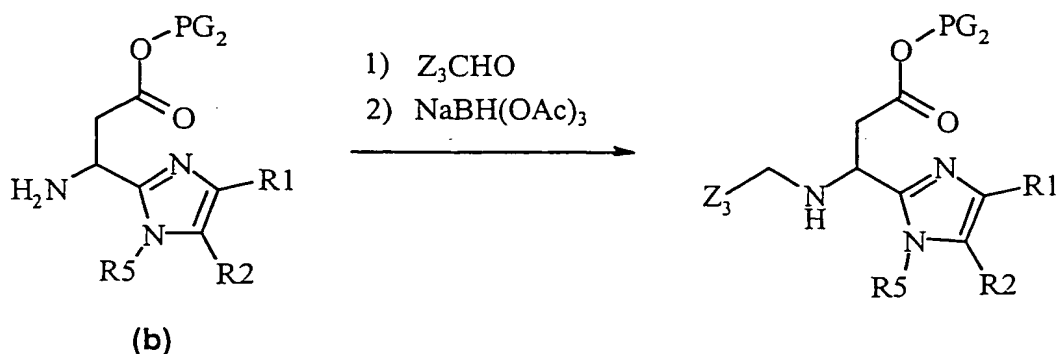
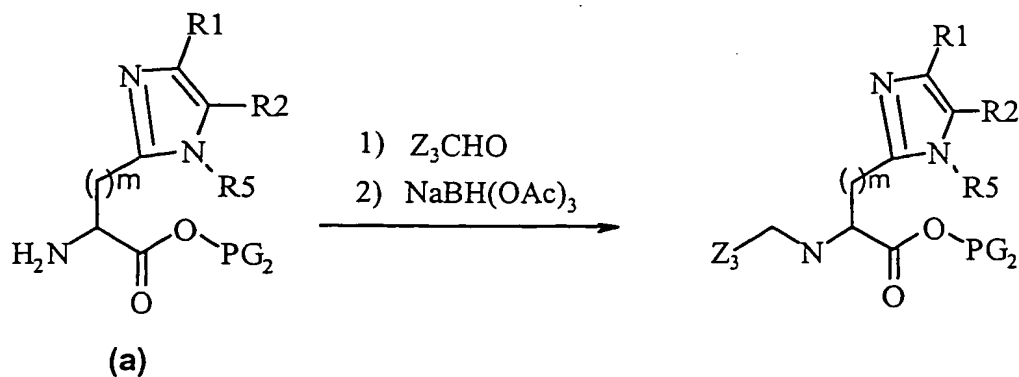
- 5 NMR (^1H , 400 MHz, DMSO- d_6): 9.21 (broad s, 2H, NH); 8.03-7.28 (m, arom. H, 11H); 5.10 (s, 1H, OCH_2Ph); 5.04 (m, 1H, CH); 3.61 (dd, 1H, CH_2 , $3J = 9 \text{ Hz}$, $2J = 17.0 \text{ Hz}$); 3.39 (dd, 1H, CH_2 , $3J = 5.5 \text{ Hz}$, $2J = 17.0 \text{ Hz}$).

MS/LC: Calculated MM = 321.2; $m/z = 322.1$ (M+H).

- 10 The following compounds are prepared in an analogous fashion to the procedure described for the dihydrochloride of benzyl (3S)-3-(4-phenyl-1H-imidazol-2-yl)-3-amino-propanoate.

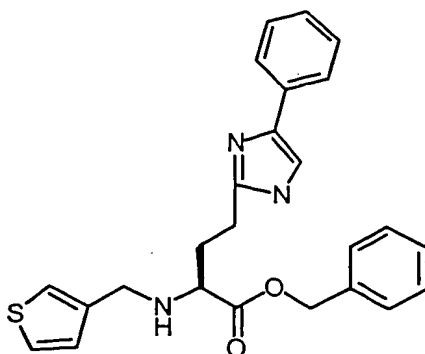


N-ALKYLATION REACTION



General procedure: A free amine of formula (a) or (b) is treated with an aldehyde in a
 5 protic or aprotic solvent, preferably dichloromethane or tetrahydrofuran, for a duration
 of 1 to 15 hours at 20-50°C. The resulting imine is then reduced using a reducing agent,
 preferably sodium triacetoxyborohydride or sodium cyanoborohydride with or without
 the presence of an acid such as acetic acid, at a temperature comprised between 20 and
 50°C for a duration of 0.2 to 5 hours. The *N*-alkylated compound is isolated by adding
 10 water and extraction followed by flash chromatography on silica gel or by
 crystallization.

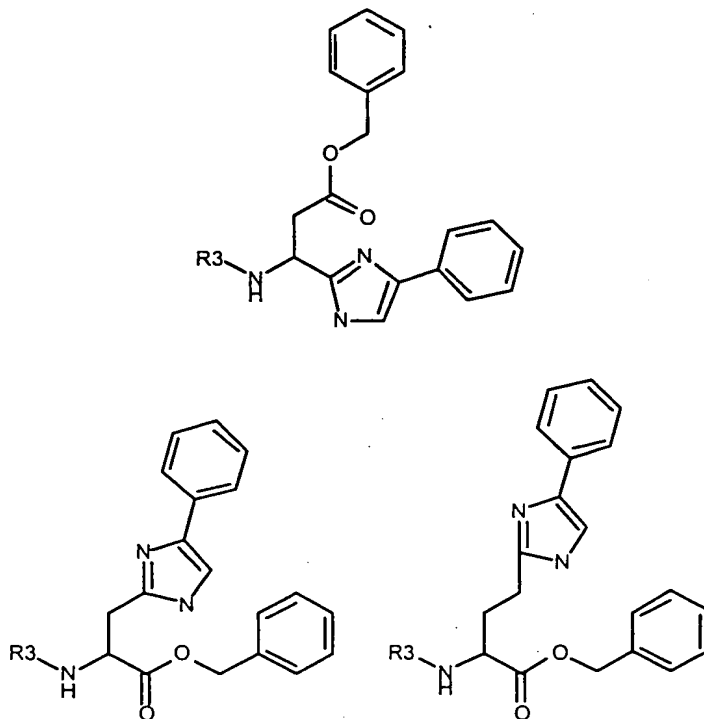
Preparation of benzyl (2S)-4-(4-phenyl-1H-imidazol-2-yl)-2-[(3-thienylmethyl)amino]butanoate



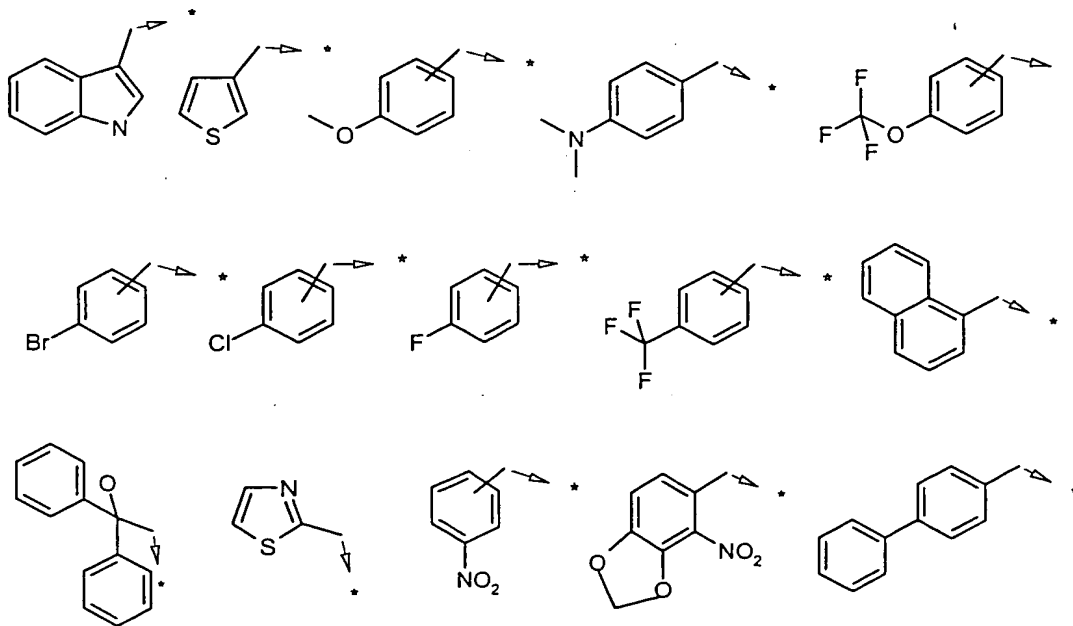
Thiophene-3-carboxaldehyde (1 ml; 1 eq.) is added to a solution of benzyl (2S)-2-amino-4-(4-phenyl-1H-imidazol-2-yl)butanoate in the form of a free base (3.6 g; 1 eq.) in tetrahydrofuran (hereafter THF, 40 ml). The mixture is stirred for 15 hours at approximately 20°C and diluted by adding 50 ml of tetrahydrofuran. NaBH(OAc)₃ (4.73 g; 2 eq.) is then added. After 1 hour of stirring at approximately 20°C, the reaction is stopped by adding water (40 ml) and ethyl acetate is then added (100 ml). After decantation and extraction, the combined organic phases are washed with salt water, dried over Na₂SO₄ then evaporated under reduced pressure at 40°C. Flash chromatography purification on silica gel (eluent: ethyl acetate / heptane 9:1) yields the expected compound in the form of a yellow oil (3.08 g; 66 % yield). NMR (¹H, 400 MHz, CDCl₃): 7.62-7.04 (m, 15H, arom. H, NH); 5.18 (s, 2H, OCH₂); 3.87-3.69 (AB, 2H, CH₂NH, 2J_{AB} = 13 Hz); 3.38 (dd, 1H, CHNH, 3J = 4.5 Hz, 2J = 8.5 Hz); 2.98 (m, 1H, CH₂CH); 2.88 (m, 1H, CH₂CH); 2.17 (m, 1H, CH₂); 1.97 (m, 1H, CH₂).

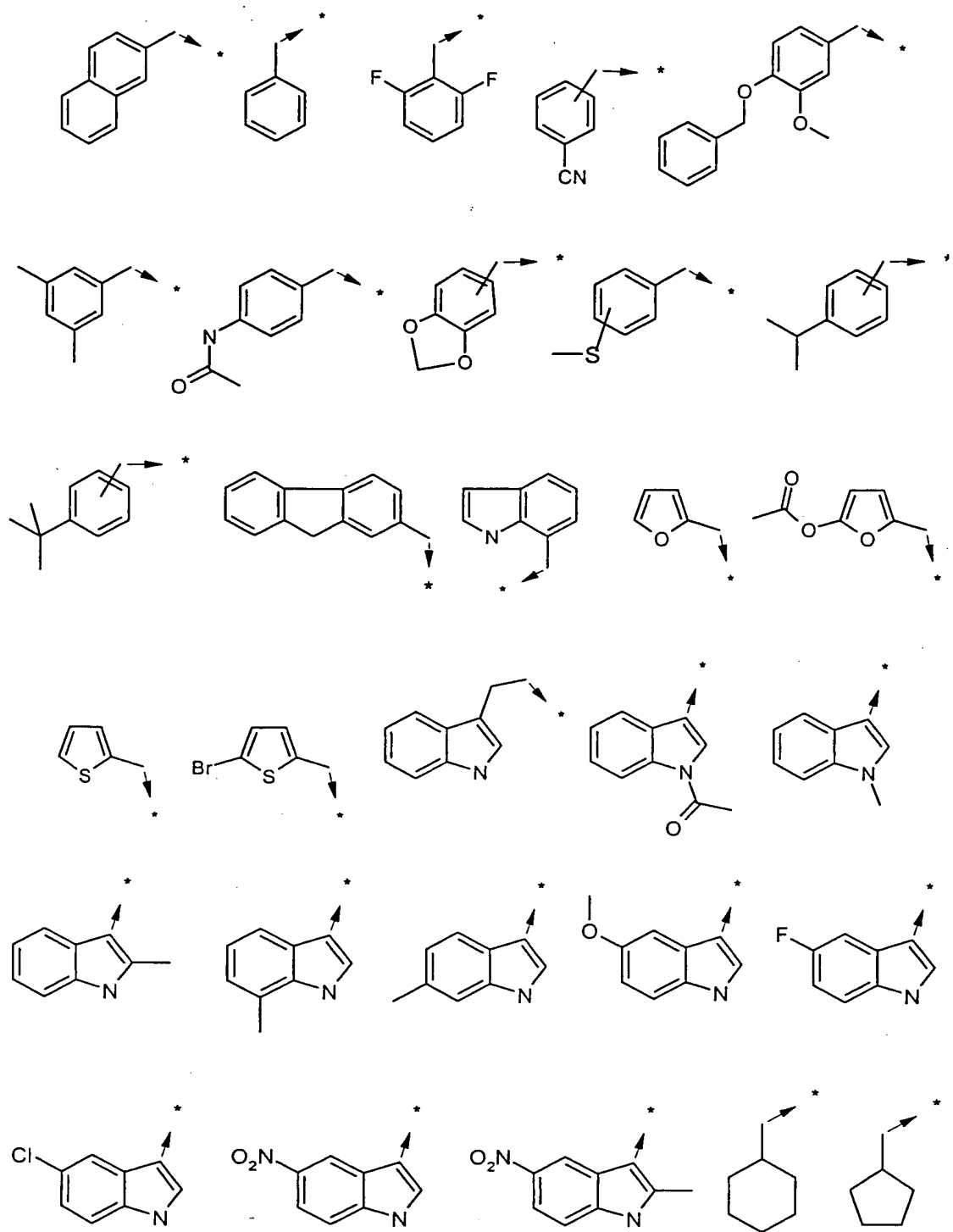
MS/LC: Calculated MM = 431.2; m/z = 432.2 (M+H); m/z = 430.8 (M-H).

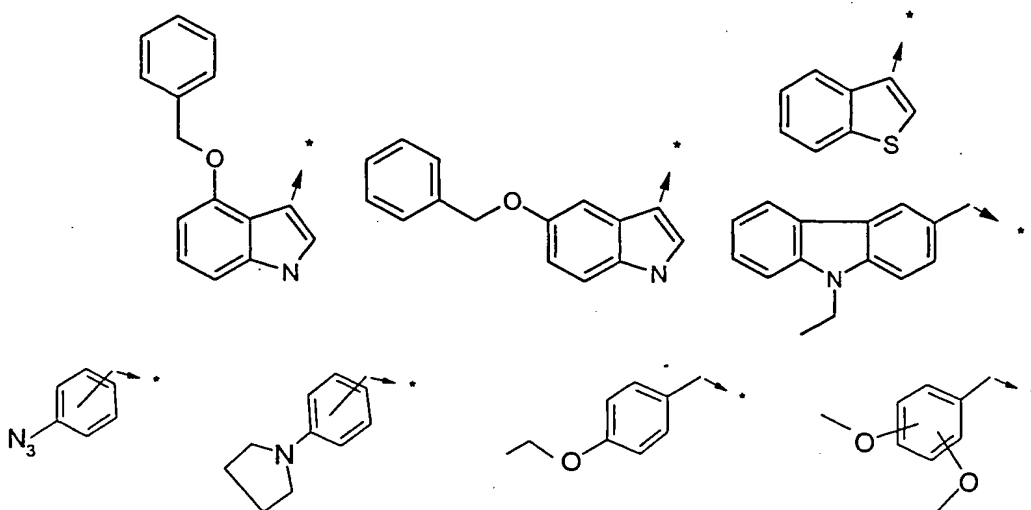
The following compounds (in their two enantiomer forms) are prepared in an analogous fashion to the procedure described for benzyl (2S)-4-(4-phenyl-1H-imidazol-2-yl)-2-[(3-thienylmethyl)amino]butanoate:



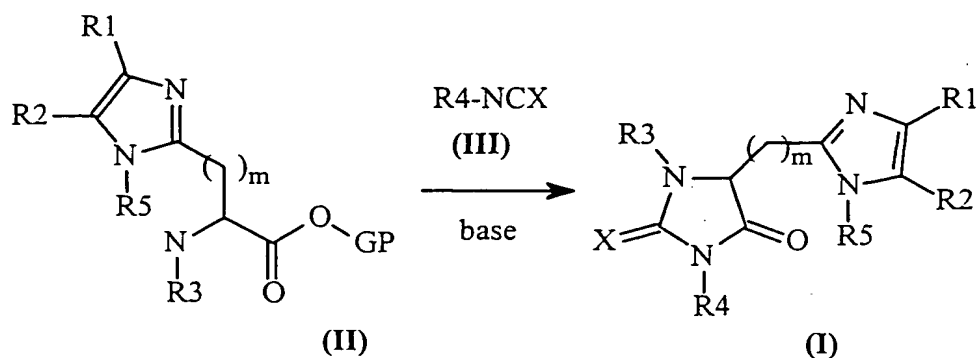
In the above formulae, R₃ represents one of the following radicals:







PREPARATION OF HYDANTOINS AND THIOHYDANTOINS



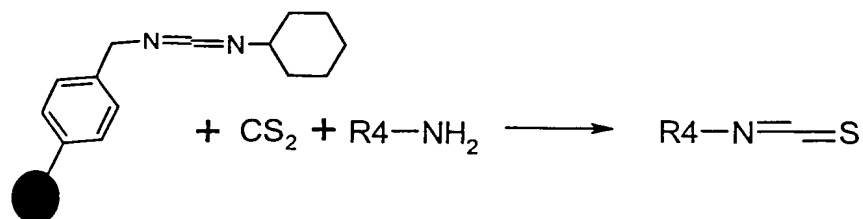
$X = O \text{ or } S ; n = 0$

General procedure:

An amine of formula (II), in which m, R1, R2, R3 and R5 have the same meanings as in general formula (I) and the O-GP radical is a parting protective group derived from an alcohol and in particular benzyloxy, methoxy or tert-butoxy, is treated with an isocyanate or a isothiocyanate of general formula R4-NCX in which R4 has the same meaning as in general formula (I), in the presence or in the absence of a tertiary base such as triethylamine or *N,N*-diisopropylethylamine, in an aprotic solvent, preferably tetrahydrofuran or dichloromethane, at a temperature comprised between approximately 20 and 60°C and for 1 to 24 hours. The resulting hydantoin or thiohydantoin can be isolated with a yield of 60 to 95 %, either by flash chromatography on silica gel or by addition to the reaction mixture of a nucleophilic reagent carried by a polymer such as for example an aminomethylpolystyrene resin (acquired from Novabiochem) followed by filtration and evaporation of the filtrate.

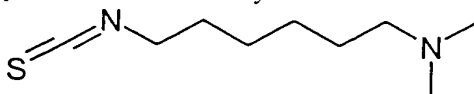
When R4 represents a radical comprising a primary amino termination (for example R4 represents aminoethyl, aminopropyl, etc.), the reagent is not R4-NCX but the corresponding compound the amino group of which is protected by a suitable protective group, for example a tert-butoxycarbonyl group. A subsequent deprotection stage (carried out under standard conditions, namely an acid treatment) must therefore be carried out in order to obtain the compound of general formula (I).

Preparation of certain non-commercial isothiocyanates of general formula (III):



These compounds are prepared as follows: a primary amine of general formula R4-NH₂ is treated with a mixture of carbon disulphide and *N*-cyclohexylcarbodiimide *N*-methyl polystyrene resin, in an aprotic solvent, preferably tetrahydrofuran or dichloromethane, for a duration of 1 hour to 18 hours at 20-50°C. The resulting isothiocyanate is isolated after filtration on frit and evaporation of the filtrate.

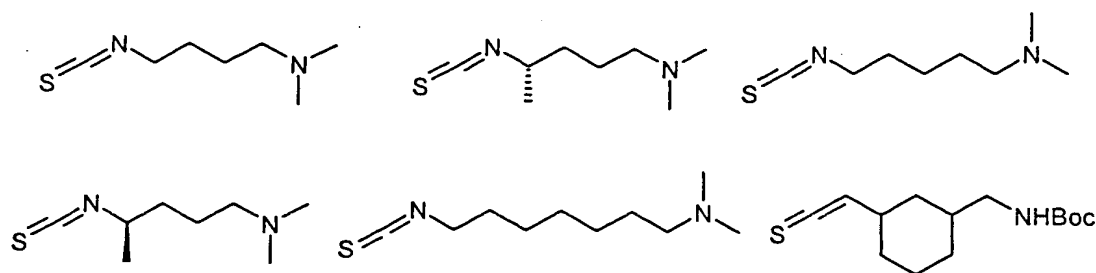
Preparation of 6-isothiocyanato-N,N-dimethyl-1-hexanamine



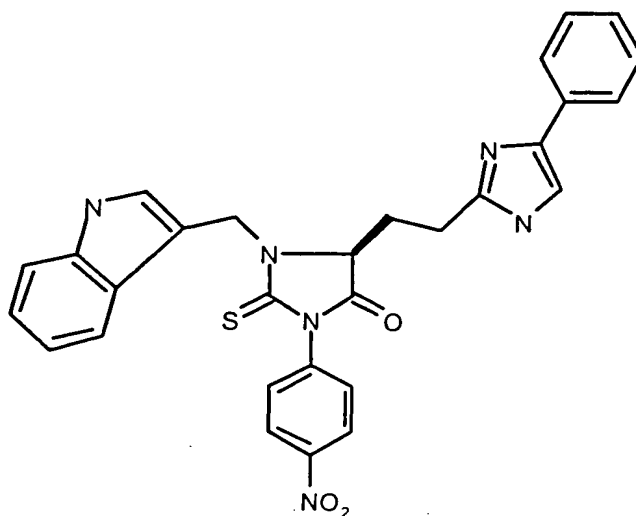
Carbon disulphide (8.3 mL, 10 eq) and a solution of *N,N*-dimethyl-1,6-hexanediamine (2g, 1 eq) in THF (10 mL) are added successively dropwise to a suspension of *N*-cyclohexylcarbodiimide *N*-methyl polystyrene resin (7.8g, 1.1 eq; acquired from Novabiochem, load 1.95 mmol/g) in anhydrous THF (120 mL). The suspension is stirred for 2 hours at approximately 20°C then filtered on frit. The filtrate is then concentrated to dryness under reduced pressure at 40°C in order to produce the expected isothiocyanate derivative (2.6g, 93% yield).

NMR ¹H, 400 MHz, CDCl₃,) : 3.50 (t, 2H); 2.24 (t, 2H), 2.20 (s, 6H), 1.68 (q, 2H), 1.50-1.31 (m, 6H).

The following compounds are prepared in an analogous fashion to the procedure described for 6-isothiocyanato-*N,N*-dimethyl-1-hexanamine:



Preparation of (5S)-1-(1H-indol-3-ylmethyl)-3-(4-nitrophenyl)-5-[2-(4-phenyl-1H-imidazol-2-yl)ethyl]-2-thioxo-4-imidazolidinone

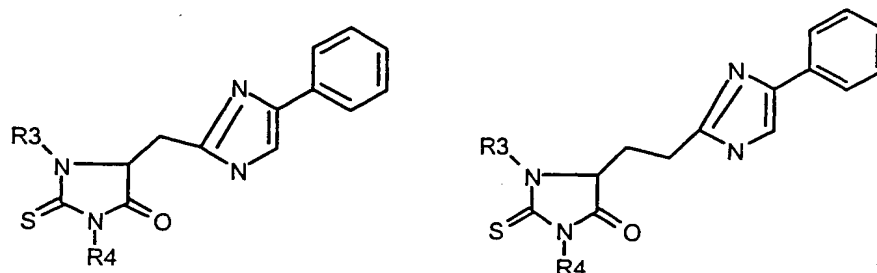


4-nitro-phenylisothiocyanate (43 mg; 1.2 eq.) is added to a solution of benzyl (2S)-2-
 5 [(1H-indol-3-ylmethyl)amino]-4-(4-phenyl-1H-imidazol-2-yl)butanoate (93 mg; 1 eq.)
 in THF (2 ml). The mixture is stirred for 2 hours at approximately 20°C then diluted
 with 4 ml of THF. Aminomethylpolystyrene resin (acquired from Novabiochem, load
 3.2 mmol/g, 125 mg, 2 eq.) is added, then triethylamine (200 μ l). The mixture is stirred
 for 15 hours at approximately 20°C then filtered on frit. The filtrate is concentrated to
 10 dryness under reduced pressure at 40°C (a co-evaporation with dichloromethane is
 necessary to eliminate the excess triethylamine). Purification of the residue by flash
 chromatography on silica gel (eluent: ethyl acetate/heptane 9:1) yields the expected
 compound (90 mg; 84 % yield).

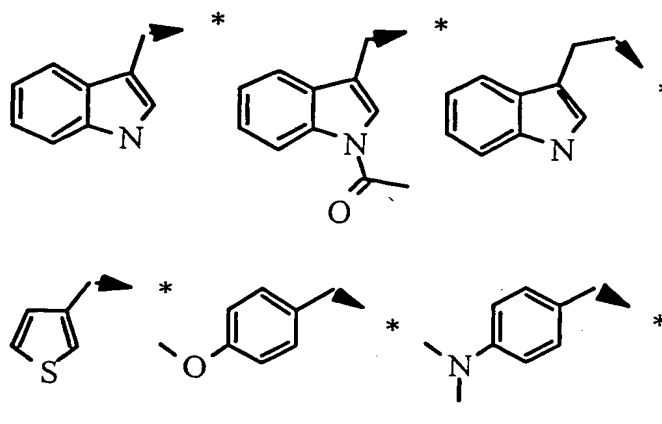
NMR (^1H , 400 MHz, CDCl_3): 8.24-7.09 (m, 17H, arom H, NH); 5.88, 4.64 (AB, 2H,
 15 CH_2N , $2J_{\text{AB}} = 15$ Hz); 3.38 (dd, 1H, CH, $3J = 3.0$ Hz, $2J = 8.5$ Hz); 2.92 (m, 2H,
 CH_2CH); 2.74 (m, 1H, CH_2); 2.24 (m, 1H, CH_2).

MS/LC: Calculated MM = 536.2; $m/z = 537.1$ (M+H).

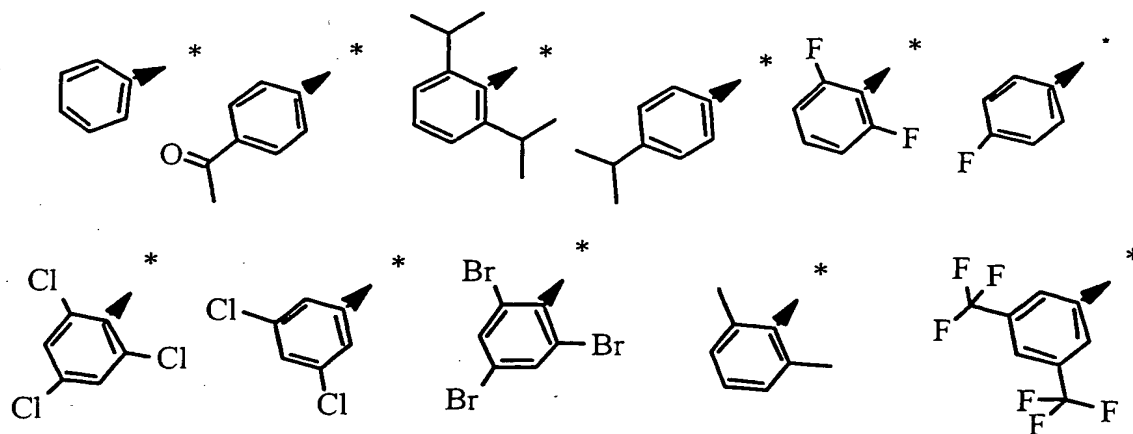
The following compounds (in their two enantiomer forms) are prepared in an analogous fashion to the procedure described for (5S)-1-(1H-indol-3-ylmethyl)-3-(4-nitrophenyl)-5-[2-(4-phenyl-1H-imidazol-2-yl)ethyl]-2-thioxo-4-imidazolidinone (apart from the final purification by flash chromatography on silica gel which is optional):

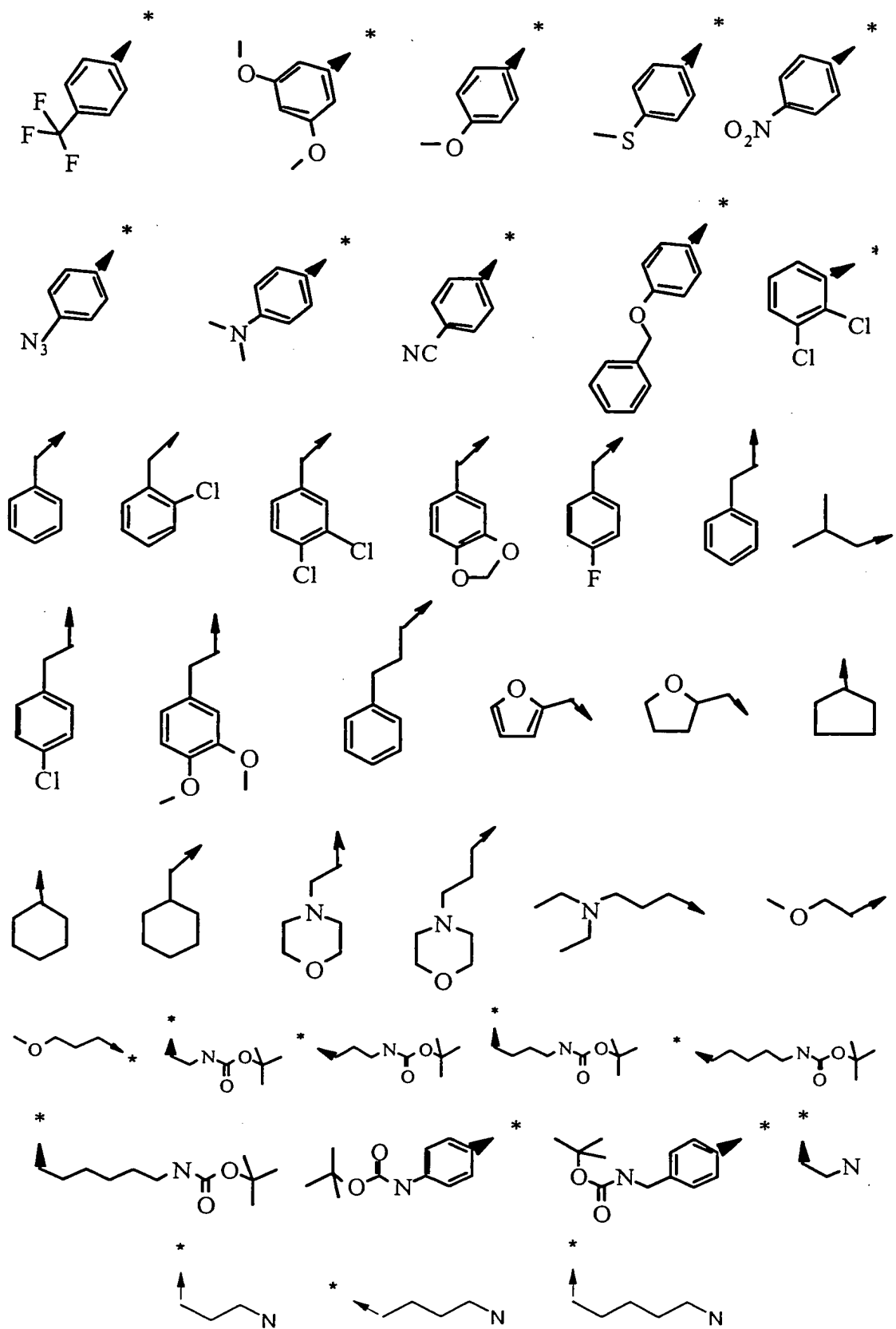


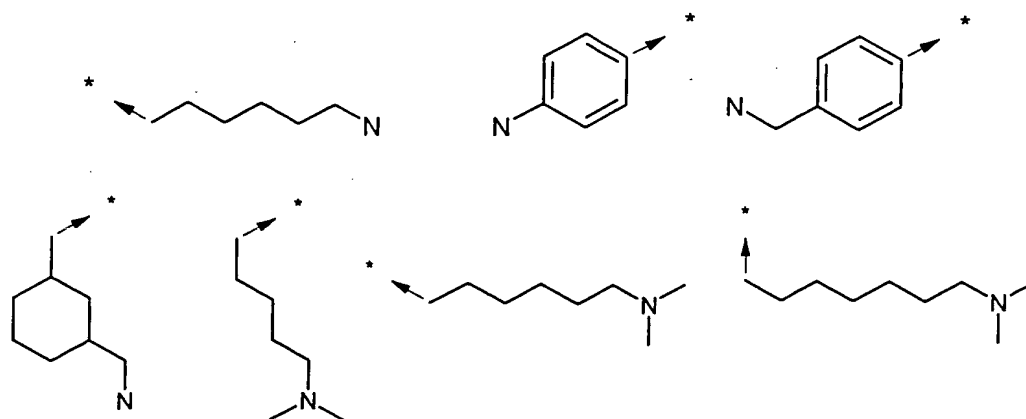
5 In the above formulae, R3 represents one of the following radicals:



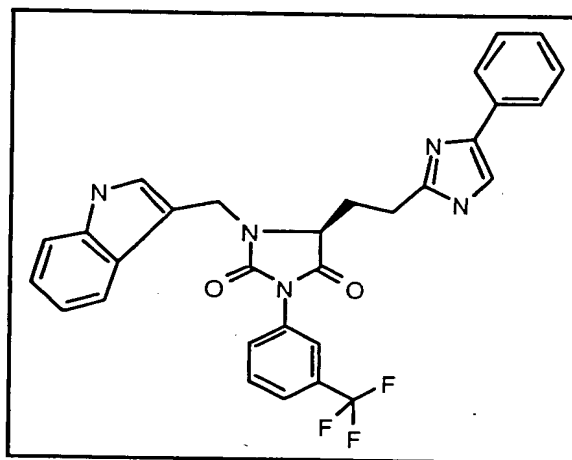
and R4 represents one of the following radicals:





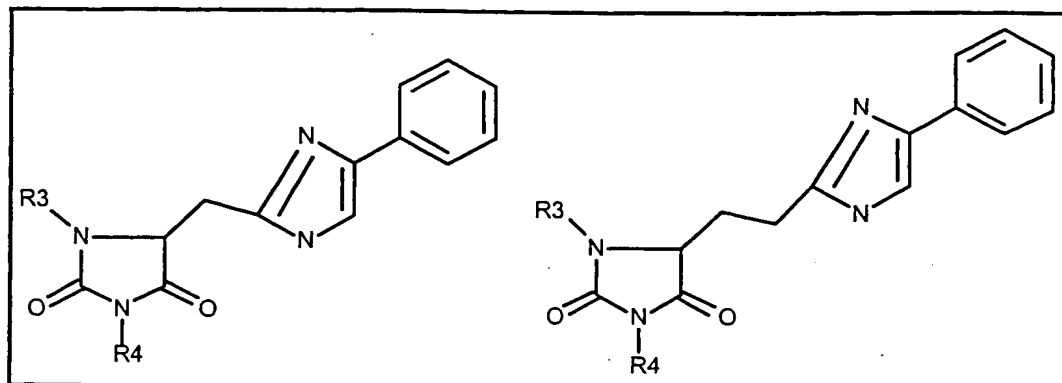


Preparation of (5S)-1-(1H-indol-3-ylmethyl)-5-[2-(4-phenyl-1H-imidazol-2-yl)ethyl]-3-[3-(trifluoromethyl)phenyl]-2,4-imidazolidinedione

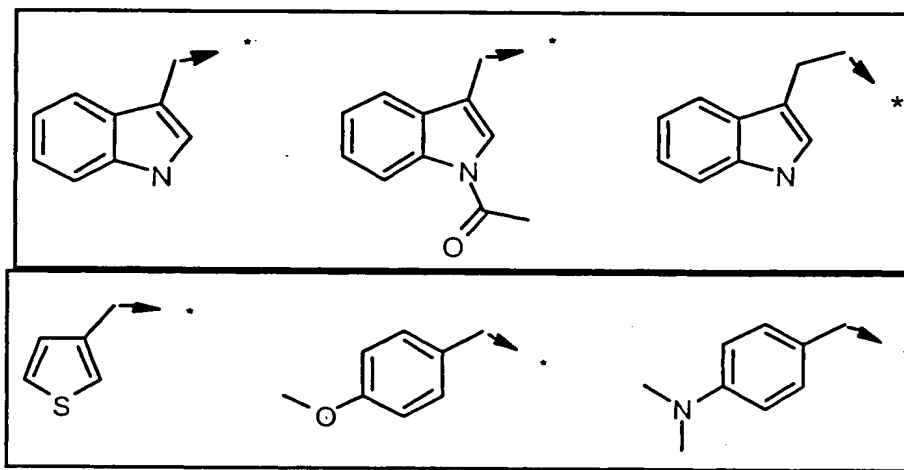


- 3-trifluoromethyl-phenylisocyanate (11 mg, 1.2 eq.) is added to a solution of benzyl (2S)-2-[(1H-indol-3-ylmethyl)amino]-4-(4-phenyl-1H-imidazol-2-yl)butanoate (23 mg, 1 eq.) in 2 ml of THF. The mixture is stirred for 2 hours at approximately 20°C then diluted with 2 ml of THF. Aminomethylpolystyrene resin (acquired from Novabiochem, load 3.2 mmol/g, 125 mg, 2 eq.) is added, then triethylamine (200 μ l). The mixture is stirred for 15 hours at approximately 20°C then filtered on frit. The filtrate is then concentrated to dryness under reduced pressure at 40°C (a co-evaporation with dichloromethane is necessary to eliminate the excess triethylamine) in order to produce the expected compound (25 mg, 92% yield).
- NMR (^1H , 400 MHz, CDCl_3): 7.75-6.99 (m, 17H, arom H, NH); 5.25, 4.44 (AB, 2H, CH_2N , $J_{\text{AB}} = 15$ Hz); 3.77 (m, 1H, CH); 2.92 (m, 1H, CH_2CH); 2.88 (m, 1H, CH_2CH); 2.72 (m, 1H, CH_2); 2.17 (m, 1H, CH_2).
- MS/LC: Calculated MM = 543.2; $m/z = 544.2$ (M+H).

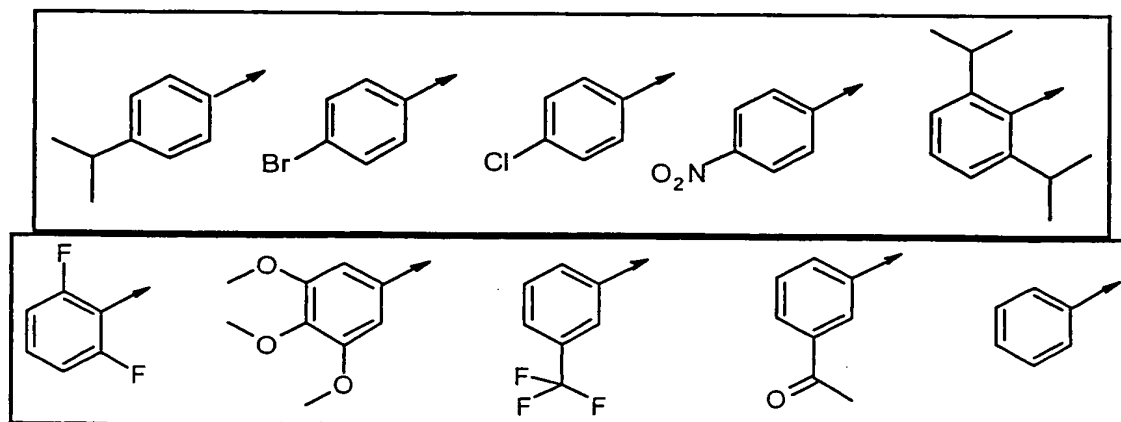
The following compounds (in their two enantiomer forms) are prepared in an analogous fashion to the procedure described for (5S)-1-(1H-indol-3-ylmethyl)-5-[2-(4-phenyl-1H-imidazol-2-yl)ethyl]-3-[3-(trifluoromethyl)phenyl]-2,4-imidazolidinedione:

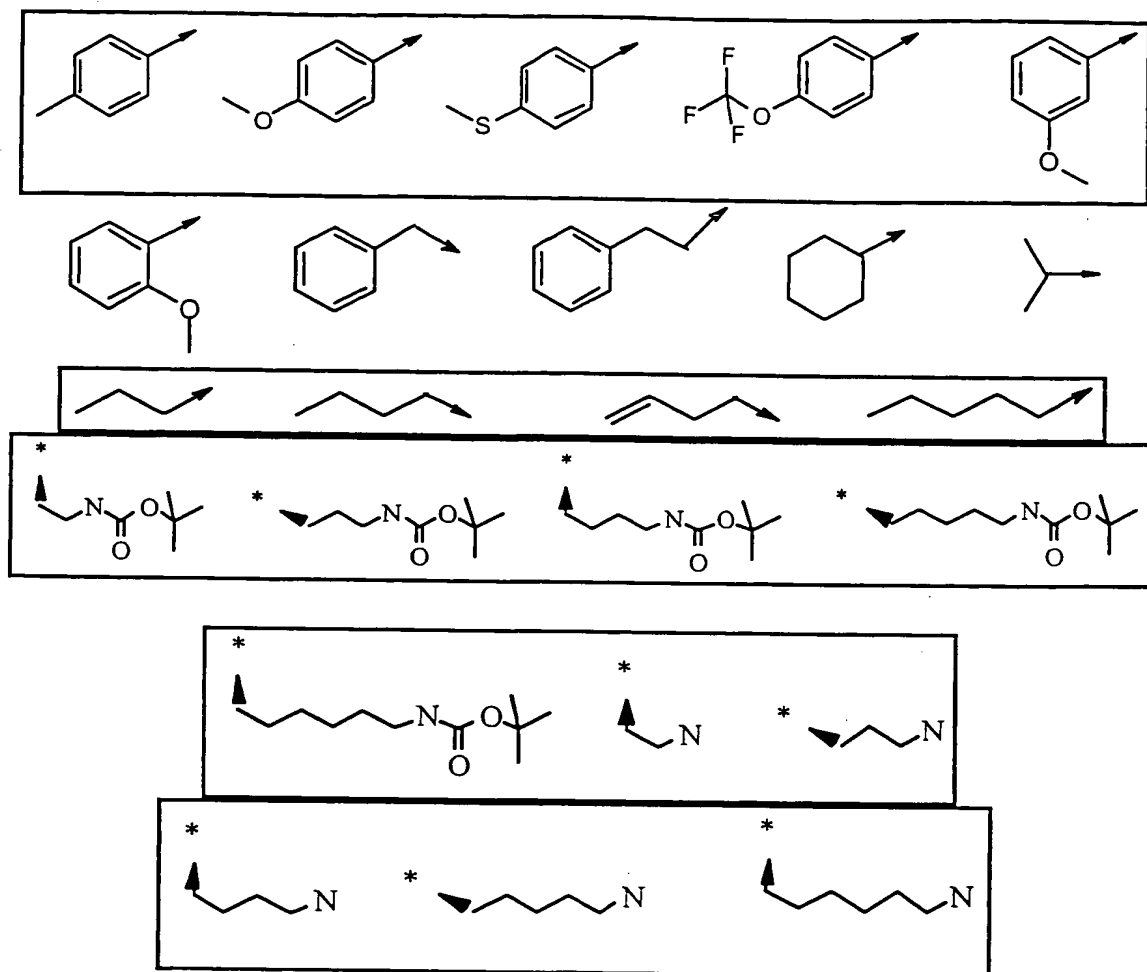


In the above formulae, R3 represents one of the following radicals:

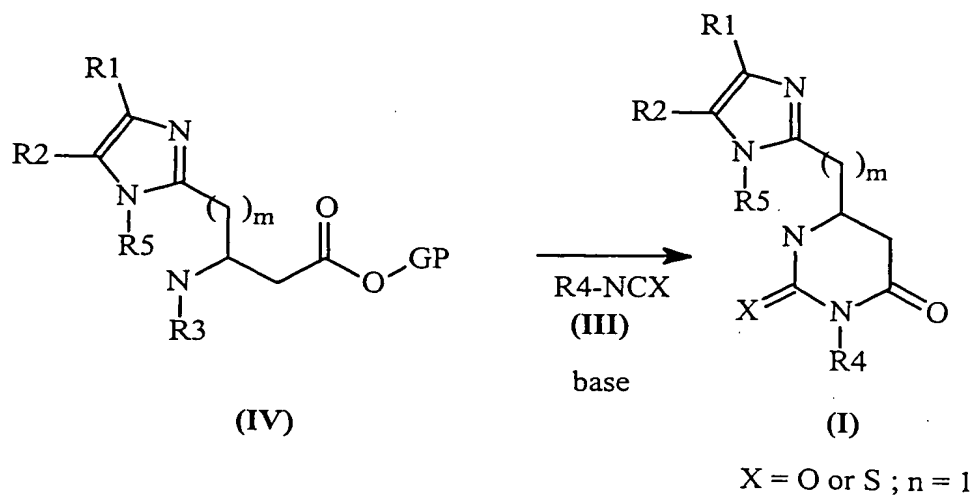


5 and R4 represents one of the following radicals:





PREPARATION OF DIHYDROPYRIMIDINE-2,4-DIONES AND 2-THIOXO-TETRAHYDRO-4-PYRIMIDINONES

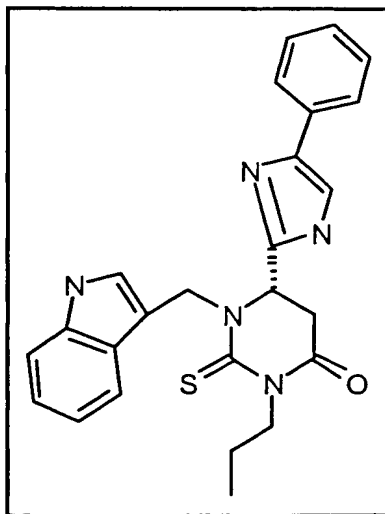


General procedure:

An amine of general formula (IV), in which m, R1, R2, R3 and R5 have the same meanings as in general formula (I) and the O-GP radical is a parting protective group derived from alcohol and in particular benzyloxy, methoxy or tert-butoxy, is treated with an isocyanate or isothiocyanate R4-NCX in the presence of a tertiary base such as triethylamine or *N,N*-diisopropylethylamine in an aprotic solvent, preferably THF or dichloromethane, at a temperature comprised between 20 and 70°C for 1 to 48 hours. The compound obtained can be isolated with a yield of 40 to 90 %, either by flash chromatography on silica gel or by addition to the reaction mixture of a nucleophilic reagent carried by a polymer such as for example an aminomethylpolystyrene resin (acquired from Novabiochem) followed by filtration and evaporation of the filtrate.

When R4 represents a radical comprising a primary amino termination (for example R4 represents aminoethyl, aminopropyl, etc.), the reagent is not R4-NCX but the corresponding compound the amino group of which is protected by a suitable protective group, for example a tert-butoxycarbonyl group. A subsequent deprotection stage (carried out under standard conditions, namely an acid treatment) must therefore be carried out in order to obtain the compound of general formula (I).

Preparation of (6S)-1-(1H-indol-3-ylmethyl)-3-propyl-6-(4-phenyl-1H-imidazol-2-yl)-2-thioxotetrahydro-4(1H)-pyrimidinone



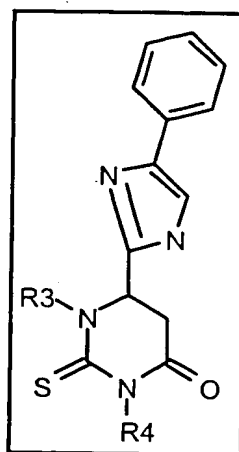
Propylisothiocyanate (25 μ l, 1.2 eq.) is added to a solution of benzyl (3*S*)-3-[(1*H*-indol-3-ylmethyl)amino]-3-(4-phenyl-1*H*-imidazol-2-yl)propanoate (90 mg, 1 eq.) in 2 ml of THF. The mixture is stirred for 15 hours at a temperature of approximately 40°C then

diluted with 2 ml of THF. An aminomethylpolystyrene resin (acquired from Novabiochem, load 3.2 mmol/g, 125 mg, 2 eq.) is added. The mixture is stirred for 5 hours at a temperature of approximately 20°C then filtered on frit. The filtrate is concentrated under reduced pressure at 40°C. 1 ml of THF and 1 ml of triethylamine are added to the residue. The mixture is stirred for 15 hours at a temperature of approximately 40°C then concentrated under reduced pressure. Purification by flash chromatography on silica gel (eluent: ethyl acetate / heptane 8:2) yields the expected compound (72 mg, yield 82%).

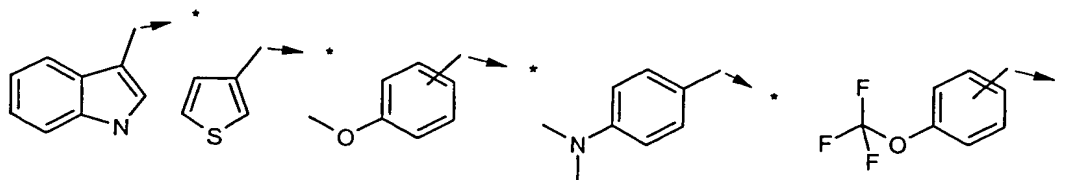
NMR (^1H , 400 MHz, CDCl_3): mixture of 2 atropisomers: 8.69-6.45 (m, 12H, H arom, NH); 6.42, 4.89 (AB, 1H, CH_2 , $J_{AB} = 14.5$ Hz); 5.78, 5.42 (AB, 1H, CH_2 , $J_{AB} = 14.5$ Hz); 4.99 (m, 1H, CH); 4.41-4.36 (m, 1H, CH_2); 4.20-4.11 (m, 1H, CH_2); 3.49, 2.94 (AB, 1H, CH_2CO , $J_{AB} = 16$ Hz); 3.28, 2.80 (AB, 1H, CH_2CO , $J_{AB} = 16$ Hz); 1.52 (m, 1H, CH_2); 1.40 (m, 1H, CH_2); 0.76, 0.62 (2m, 3H, CH_3).

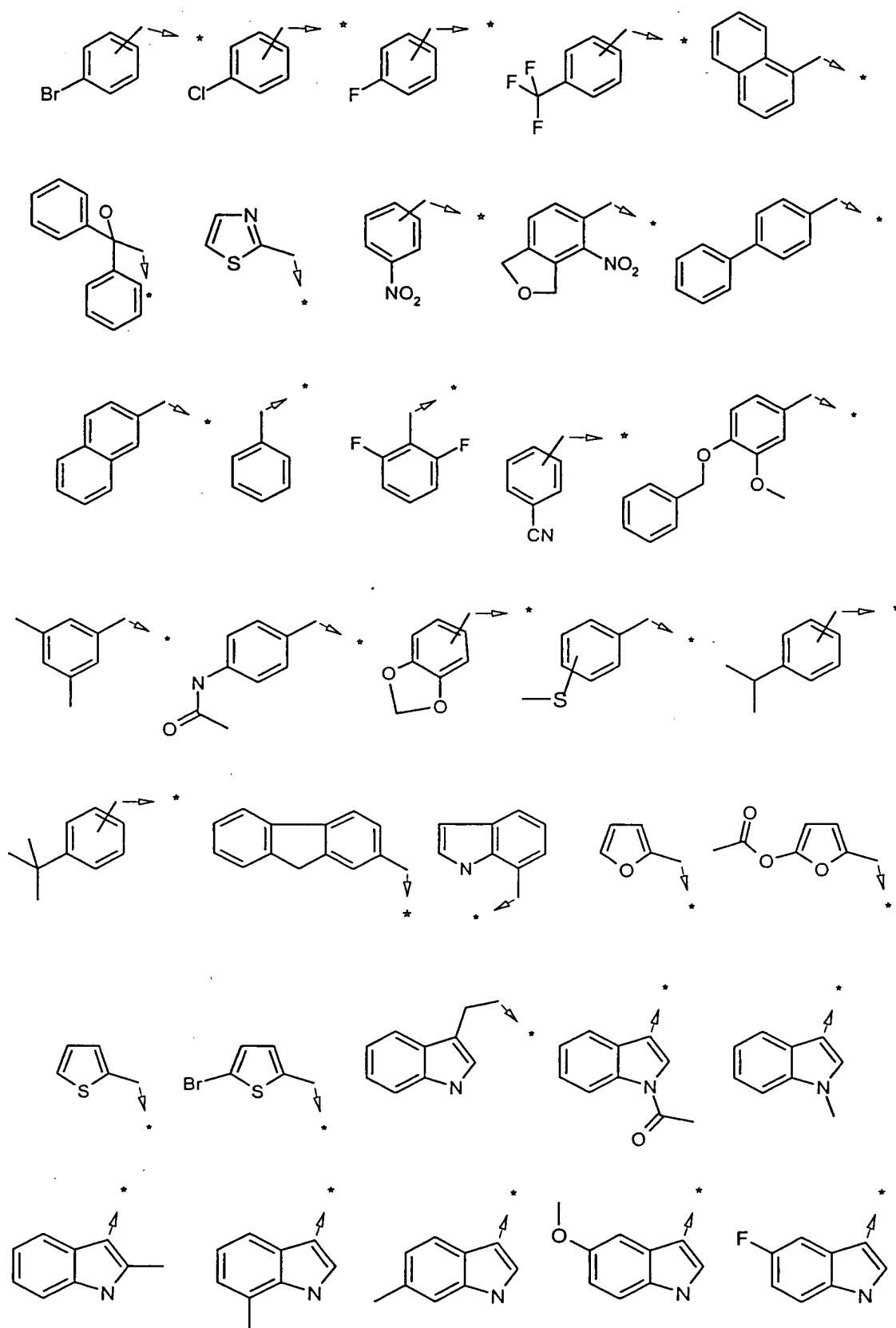
MS/LC: Calculated MM = 443.2; $m/z = 444.2$ (M+H).

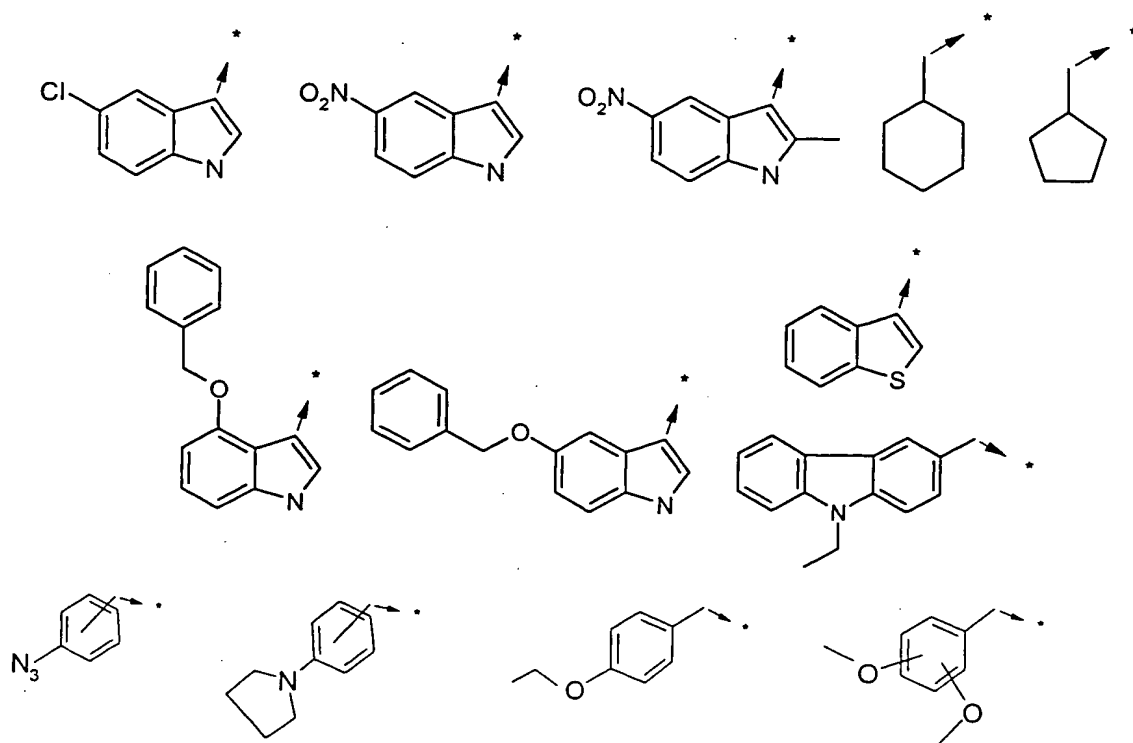
- 15 The following compounds (in their two enantiomer forms) are prepared in an analogous fashion to the procedure described for (6S)-1-(1H-indol-3-ylmethyl)-3-propyl-6-(4-phenyl-1H-imidazol-2-yl)-2-thioxotetrahydro-4(1H)-pyrimidinone (except for the final purification by flash chromatography on silica gel which is optional):



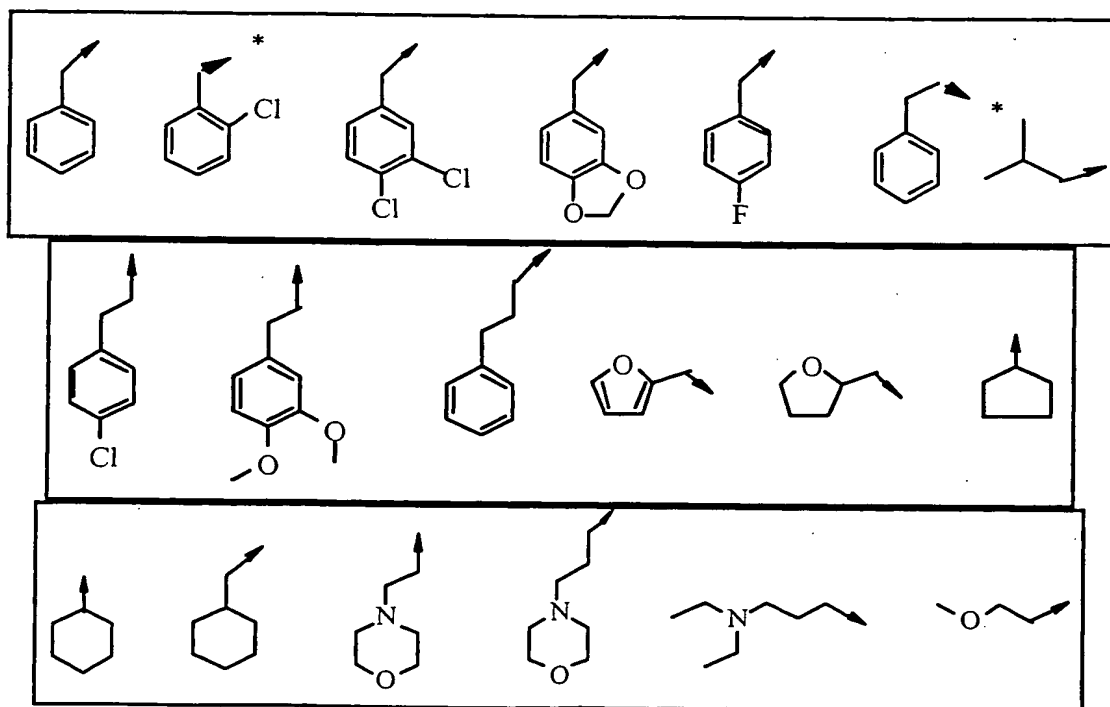
In the above formula, R3 represents one of the following radicals:

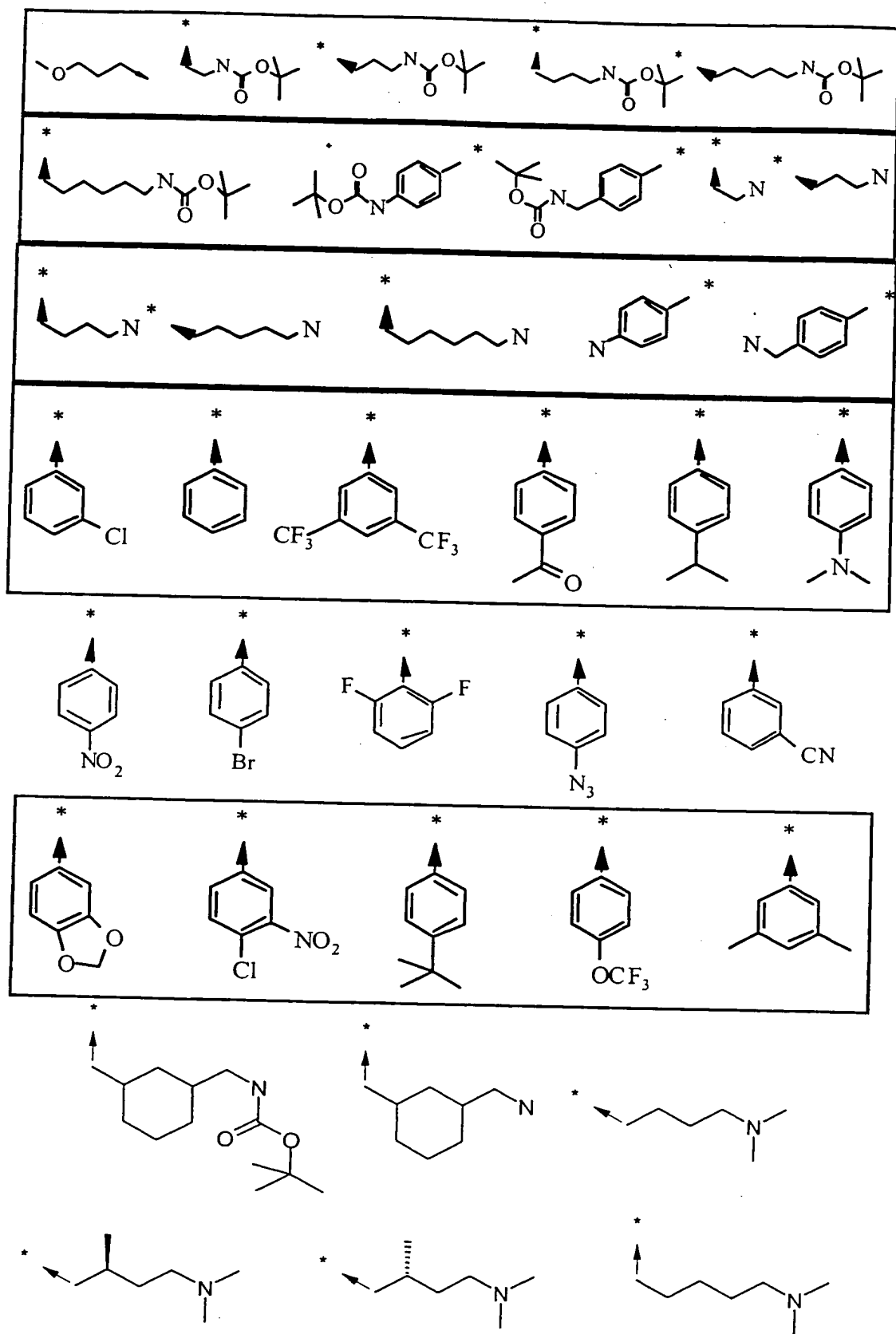


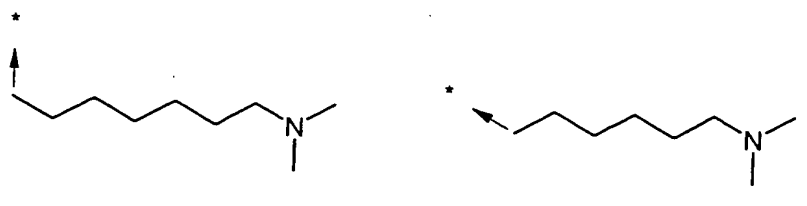




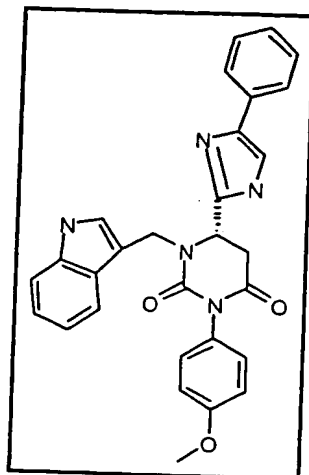
and R4 represents one of the following radicals:







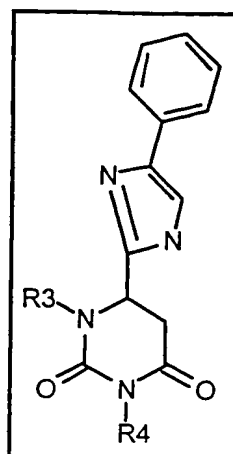
Preparation of (6S)-1-(1H-indol-3-ylmethyl)-3-(4-methoxyphenyl)-6-(4-phenyl-1H-imidazol-2-yl)dihydro-2,4(1H,3H)-pyrimidinedione



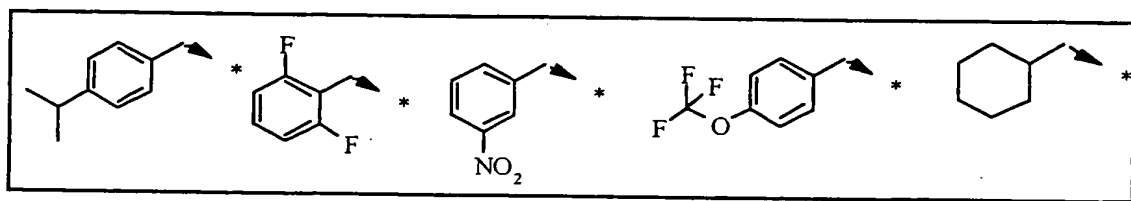
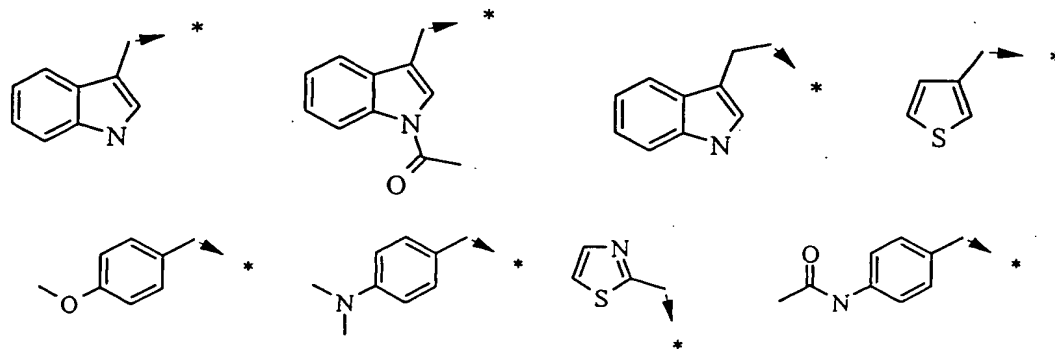
- 4-methoxyphenylisocyanate (40 μ l, 1.2 eq.) is added to a solution of benzyl (3S)-3-
 5 [(1H-indol-3-ylmethyl)amino]-3-(4-phenyl-1H-imidazol-2-yl)propanoate (100 mg, 1
 eq.) in THF (2 ml). The mixture is stirred for 5 hours at a temperature of approximately
 20°C then diluted with 2 ml of THF. An aminomethylpolystyrene resin (acquired from
 Novabiochem, load 3.2 mmol/g, 138 mg, 2 eq.) is added. The mixture is stirred for 3
 hours at a temperature of approximately 20°C then filtered on frit. The filtrate is
 10 concentrated under reduced pressure at 40°C. 2 ml of THF and 2 ml of triethylamine are
 added to the residue. The mixture is taken to reflux for 24 hours then concentrated
 under reduced pressure. Purification of the residue by flash chromatography on silica
 gel (eluent: ethyl acetate / heptane 8:2) yields the expected compound (80 mg, yield 74
 %).
- 15 NMR (^1H , 400 MHz, CDCl_3): mixture of 2 atropisomers: 9.67-8.96 (2s, 1H, NH); 8.49
 (s, 1H, NH); 5.15, 4.36 (AB, 1H, CH_2 , $J_{\text{AB}} = 15$ Hz); 5.08, 4.69 (AB, 1H, CH_2 , $J_{\text{AB}} = 15$
 Hz); 4.67, 4.57 (2m, 1H, CH); 3.72 (s, 3H, OCH_3); 3.29-2.79 (m, 2H, CH_2CO).
 MS/LC: Calculated MM = 491.2; m/z = 492.3 (M+H).

The following compounds (in their two enantiomer forms) are prepared in an analogous
 20 fashion to the procedure described for (6S)-1-(1H-indol-3-ylmethyl)-3-(4-

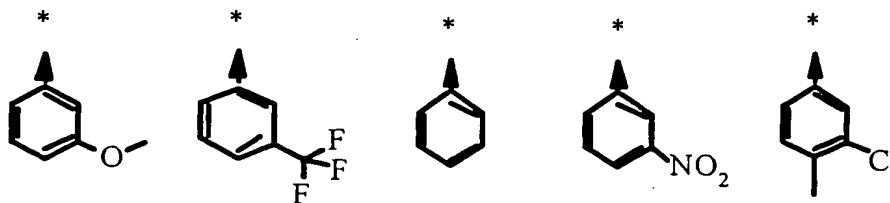
methoxyphenyl)-6-(4-phenyl-1H-imidazol-2-yl) dihydro-2,4(1H,3H)-pyrimidinedione (except for the final purification by flash chromatography on silica gel which is optional):

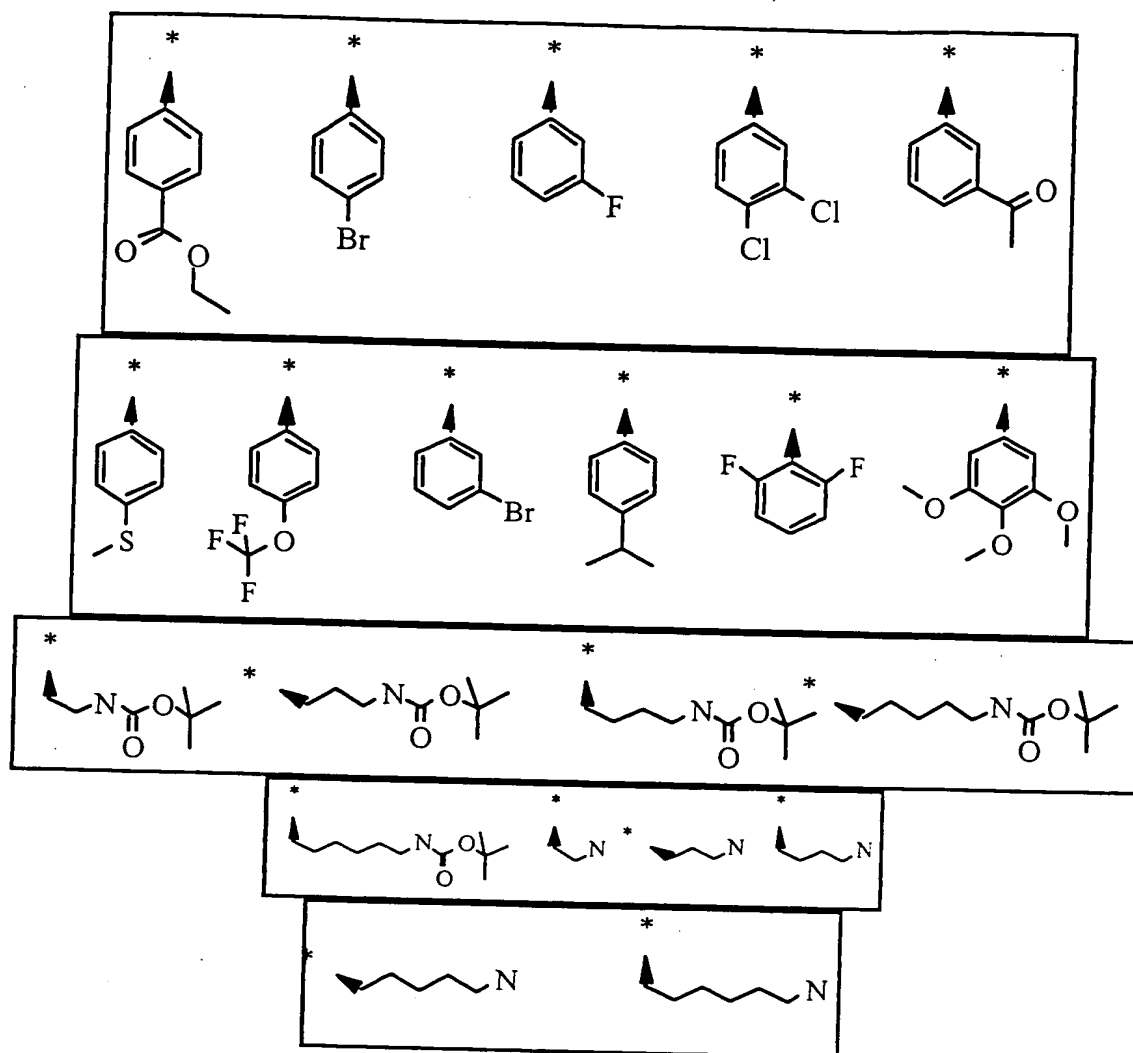


In the above formula, R3 represents one of the following radicals:



5 and R4 represents one of the following radicals:





EXAMPLES

The examples prepared according to the synthesis methods described above are shown in tables below. These examples are presented to illustrate the above procedures and should in no case be considered as limiting the scope of the invention.

Analytical methods used for the characterization of the compounds

The compounds obtained have been characterized according to their retention time (rt) and to their mass spectrometry (MH⁺).

) *Mass spectrometry*

- 5 For the mass spectrometry, a single quadrupole mass spectrometer (Micromass, platform model) equipped with an *electrospray* source is used with a resolution of 0.8 Da at 50 % valley.

Calibration is carried out monthly between the masses 80 and 1000 Da using a calibration mixture of sodium and rubidium iodide in solution in an isopropanol/water mixture (1/1 Vol.).

10

) *High performance liquid chromatography (HPLC)*

For the liquid chromatography, an HPLC HP1100 system (Hewlett-Packard) including an in-line degasser, a quaternary pump, a column oven and a diode array UV detector is used.

- 15 Different elution conditions are used according to the examples:

- Conditions (i):

Eluants:	A	water + 0.04 % trifluoroacetic acid
	B	acetonitrile

T(min)	A%	B%
0	100	0
1	100	0
8	30	70
10	30	70

Flow rate: 1.1 ml / min

Injection: 5 µl

Column: Uptisphere ODS 3µm 33*4.6 mm i.d.

Temperature: 40 °C

- Conditions (ii):

Eluants: **A** water + 0.04 % trifluoroacetic acid

B acetonitrile

T(min)	A%	B%
0	90	10
6	15	85
10	15	85

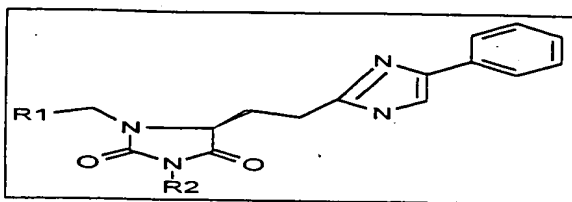
Flow rate: 1 ml / min

Injection: 5 μ l

5 Column: Uptisphere ODS 3 μ m 50*4.6 mm i.d.

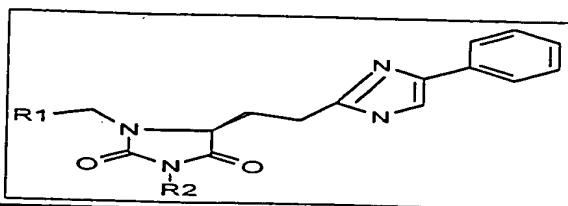
Temperature: 40 °C

Elution conditions (i) are used for the characterization of Examples 1 to 479, 560 to 572 and 733 to 1040. As regards conditions (ii) they are used for Examples 480 to 559, 573 to 732 and 1041 to 1234. The UV detection is carried out at a wavelength of 220 nm for all the examples.

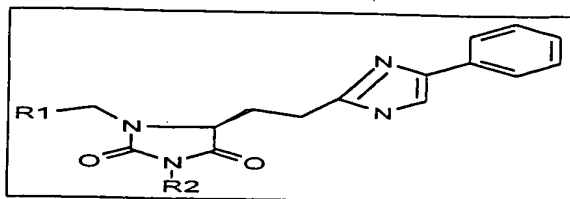


Analyses		

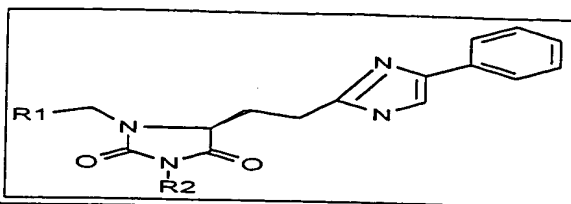
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
1	C ₂₉ H ₂₅ N ₅ O ₂			89.6%	6.2	476.2
2	C ₃₀ H ₂₇ N ₅ O ₂			91.0%	6.4	490.3
3	C ₃₀ H ₂₇ N ₅ O ₃			90.1%	6.2	506.3
4	C ₃₀ H ₂₇ N ₅ O ₂ S			91.0%	6.6	522.2
5	C ₃₀ H ₂₄ F ₃ N ₅ O ₃			83.1%	7.0	560.2
6	C ₃₂ H ₃₁ N ₅ O ₂			84.9%	7.0	518.3
7	C ₂₉ H ₂₄ BrN ₅ O ₂			81.9%	6.7	556.1
8	C ₂₉ H ₂₄ ClN ₅ O ₂			79.1%	6.6	510.2
9	C ₂₉ H ₂₄ N ₆ O ₄			87.3%	6.4	521.2
10	C ₃₅ H ₃₇ N ₅ O ₂			94.1%	7.3	560.3
11	C ₂₉ H ₂₃ F ₂ N ₅ O ₂			96.9%	6.3	512.2
12	C ₃₀ H ₂₇ N ₅ O ₂			96.3%	6.4	490.2
13	C ₃₁ H ₂₉ N ₅ O ₂			92.0%	6.5	504.2
14	C ₂₉ H ₃₁ N ₅ O ₂			85.7%	6.6	482.3
15	C ₂₆ H ₂₇ N ₅ O ₂			94.2%	5.9	442.3



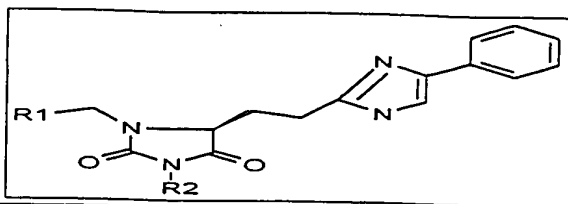
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
16	C27H29N5O2			91.7%	6.3	456.3
17	C26H25N5O2			96.6%	5.8	440.2
18	C28H31N5O2			87.2%	6.6	470.3
19	C26H27N5O2			89.1%	6.0	442.2
20	C32H31N5O5			80.5%	6.1	566.2
21	C25H22N4O2S			92.3%	5.9	443.2
22	C26H24N4O2S			90.2%	6.2	457.2
23	C26H24N4O3S			92.1%	6.0	473.2
24	C26H24N4O2S2			92.8%	6.4	489.2
25	C26H21F3N4O3S			87.7%	6.8	527.2
26	C28H28N4O2S			87.8%	6.8	485.3
27	C25H21BrN4O2S			84.3%	6.5	523.1
28	C25H21ClN4O2S			84.9%	6.4	477.2
29	C25H21N5O4S			94.0%	6.2	488.2
30	C31H34N4O2S			97.2%	7.2	527.3



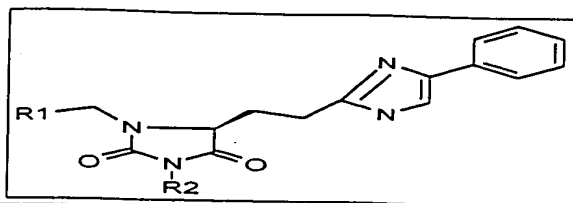
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
31	C ₂₅ H ₂₀ F ₂ N ₄ O ₂ S			96.7%	6.1	479.2
32	C ₂₆ H ₂₄ N ₄ O ₂ S			95.3%	6.2	457.2
33	C ₂₇ H ₂₆ N ₄ O ₂ S			93.0%	6.4	471.2
34	C ₂₅ H ₂₈ N ₄ O ₂ S			88.3%	6.4	449.2
35	C ₂₂ H ₂₄ N ₄ O ₂ S			90.8%	5.7	409.2
36	C ₂₃ H ₂₆ N ₄ O ₂ S			91.8%	6.1	423.2
37	C ₂₂ H ₂₂ N ₄ O ₂ S			97.9%	5.6	407.2
38	C ₂₄ H ₂₈ N ₄ O ₂ S			84.3%	6.4	437.2
39	C ₂₂ H ₂₄ N ₄ O ₂ S			87.2%	5.7	409.2
40	C ₂₈ H ₂₈ N ₄ O ₅ S			92.2%	5.9	533.2
41	C ₂₈ H ₂₆ N ₄ O ₃			93.9%	6.1	467.2
42	C ₂₉ H ₂₈ N ₄ O ₃			95.8%	6.3	481.3
43	C ₂₉ H ₂₈ N ₄ O ₄			93.0%	6.1	497.3
44	C ₂₉ H ₂₈ N ₄ O ₃ S			94.5%	6.5	513.2
45	C ₂₉ H ₂₅ F ₃ N ₄ O ₄			90.4%	6.9	551.2



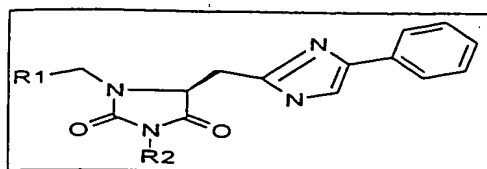
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
46	C ₃₁ H ₃₂ N ₄ O ₃			87.7%	6.9	509.3
47	C ₂₈ H ₂₅ BrN ₄ O ₃			84.2%	6.6	547.1
48	C ₂₈ H ₂₅ ClN ₄ O ₃			86.6%	6.5	501.2
49	C ₂₈ H ₂₅ N ₅ O ₅			93.9%	6.3	512.2
50	C ₃₄ H ₃₈ N ₄ O ₃			98.3%	7.2	551.3
51	C ₂₈ H ₂₄ F ₂ N ₄ O ₃			98.0%	6.2	503.2
52	C ₂₉ H ₂₈ N ₄ O ₃			94.6%	6.4	481.2
53	C ₃₀ H ₃₀ N ₄ O ₃			91.5%	6.4	495.3
54	C ₂₈ H ₃₂ N ₄ O ₃			85.8%	6.5	473.3
55	C ₂₅ H ₂₈ N ₄ O ₃			89.7%	5.8	433.3
56	C ₂₆ H ₃₀ N ₄ O ₃			90.6%	6.2	447.3
57	C ₂₅ H ₂₆ N ₄ O ₃			97.1%	5.7	431.2
58	C ₂₇ H ₃₂ N ₄ O ₃			75.3%	6.5	461.3
59	C ₂₅ H ₂₈ N ₄ O ₃			86.1%	5.9	433.3
60	C ₃₁ H ₃₂ N ₄ O ₆			83.5%	6.0	557.2



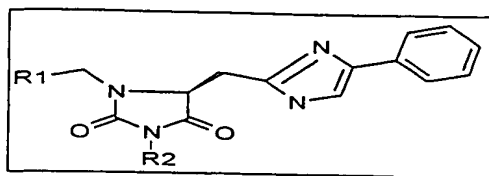
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
61	C ₂₉ H ₂₉ N ₅ O ₂			92.62%*	5.3	480.3
62	C ₃₀ H ₃₁ N ₅ O ₂			93.25%*	5.6	494.3
63	C ₃₀ H ₃₁ N ₅ O ₃			94.39%*	5.4	510.3
64	C ₃₀ H ₃₁ N ₅ O ₂ S			95.36%*	5.8	526.3
65	C ₃₀ H ₂₈ F ₃ N ₅ O ₃			89.2%	6.3	564.2
66	C ₃₂ H ₃₅ N ₅ O ₂			86.35%*	6.3	522.3
67	C ₂₉ H ₂₈ BrN ₅ O ₂			84.14%*	5.9	560.1
68	C ₂₉ H ₂₈ ClN ₅ O ₂			85.8%	5.8	514.2
69	C ₂₉ H ₂₈ N ₆ O ₄			94.4%	5.6	525.3
70	C ₃₅ H ₄₁ N ₅ O ₂			95.76%*	6.8	564.3
71	C ₂₉ H ₂₇ F ₂ N ₅ O ₂			96.29%*	5.5	516.3
72	C ₃₀ H ₃₁ N ₅ O ₂			97.59%*	5.6	494.3
73	C ₃₁ H ₃₃ N ₅ O ₂			94.87%*	5.7	508.3
74	C ₂₉ H ₃₅ N ₅ O ₂			87.63%*	5.8	486.3
75	C ₂₆ H ₃₁ N ₅ O ₂			87.69%*	5.0	446.3



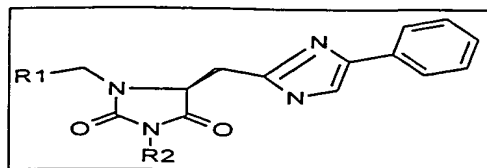
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
76	C ₂₇ H ₃₃ N ₅ O ₂			86.66%*	5.4	460.3
77	C ₂₆ H ₂₉ N ₅ O ₂			93.78%*	4.9	444.3
78	C ₂₈ H ₃₅ N ₅ O ₂			85%*	5.8	474.3
79	C ₂₆ H ₃₁ N ₅ O ₂			87.49%*	5.0	446.3
80	C ₃₂ H ₃₅ N ₅ O ₅			87.6%	5.3	570.3



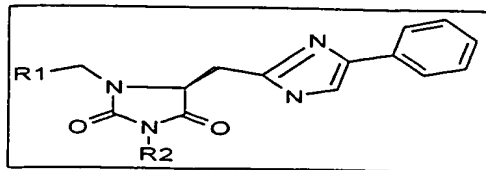
Analyses						
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
81	C ₂₈ H ₂₃ N ₅ O ₂			92%	6.2	462.2
82	C ₂₉ H ₂₅ N ₅ O ₂			93%	6.5	476.2
83	C ₂₉ H ₂₅ N ₅ O ₃			94%	6.2	492.2
84	C ₂₉ H ₂₅ N ₅ O ₂ S			92%	6.6	508.2
85	C ₂₉ H ₂₂ F ₃ N ₅ O ₃			92%	7.0	546.2
86	C ₃₁ H ₂₉ N ₅ O ₂			92%	7.1	504.3
87	C ₂₈ H ₂₂ BrN ₅ O ₂			92%	6.8	542.1
88	C ₂₈ H ₂₂ ClN ₅ O ₂			92%	6.7	496.2
89	C ₂₈ H ₂₂ N ₆ O ₄			82%	6.5	507.2
90	C ₃₄ H ₃₅ N ₅ O ₂			92%	7.3	546.3
91	C ₂₈ H ₂₁ F ₂ N ₅ O ₂			90%	6.2	498.2
92	C ₃₁ H ₂₉ N ₅ O ₅			82%	6.2	552.2
93	C ₂₉ H ₂₂ F ₃ N ₅ O ₂			92%	6.9	530.2
94	C ₃₀ H ₂₅ N ₅ O ₃			89%	6.1	504.2
95	C ₂₉ H ₂₅ N ₅ O ₂			92%	6.4	476.2



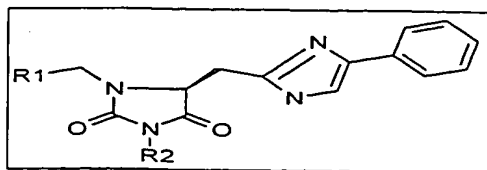
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
96	C30H27N5O2			93%	6.6	490.3
97	C25H25N5O2			95%	5.9	428.2
98	C26H27N5O2			95%	6.3	442.3
99	C25H23N5O2			95%	5.8	426.2
100	C27H29N5O2			94%	6.6	456.3
101	C24H20N4O2S			92%	5.9	429.2
102	C25H22N4O2S			91%	6.2	443.2
103	C25H22N4O3S			90%	6.0	459.2
104	C25H22N4O2S2			87%	6.4	475.2
105	C25H19F3N4O3S			89%	6.8	513.2
106	C27H26N4O2S			89%	6.9	471.2
107	C24H19BrN4O2S			91%	6.5	509.1
108	C24H19ClN4O2S			90%	6.4	463.1
109	C24H19N5O4S			76%	6.3	474.2
110	C30H32N4O2S			90%	7.1	513.3



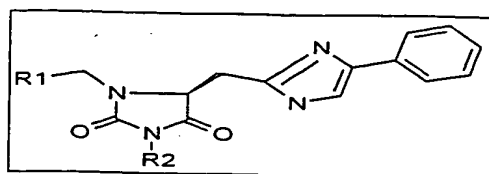
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
111	C ₂₄ H ₁₈ F ₂ N ₄ O ₂ S			82%	6.0	465.2
112	C ₂₇ H ₂₆ N ₄ O ₅ S			77%	5.8	519.2
113	C ₂₅ H ₁₉ F ₃ N ₄ O ₂ S			89%	6.7	497.2
114	C ₂₆ H ₂₂ N ₄ O ₃ S			86%	5.8	471.2
115	C ₂₅ H ₂₂ N ₄ O ₂ S			85%	6.1	443.2
116	C ₂₆ H ₂₄ N ₄ O ₂ S			82%	6.3	457.2
117	C ₂₁ H ₂₂ N ₄ O ₂ S			84%	5.6	395.2
118	C ₂₂ H ₂₄ N ₄ O ₂ S			93%	5.9	409.2
119	C ₂₁ H ₂₀ N ₄ O ₂ S			89%	5.4	393.2
120	C ₂₃ H ₂₆ N ₄ O ₂ S			81%	6.3	423.2
121	C ₂₇ H ₂₄ N ₄ O ₃			91%	6.0	453.2
122	C ₂₈ H ₂₆ N ₄ O ₃			92%	6.3	467.2
123	C ₂₈ H ₂₆ N ₄ O ₄			91%	6.0	483.3
124	C ₂₈ H ₂₆ N ₄ O ₃ S			88%	6.4	499.2
125	C ₂₈ H ₂₃ F ₃ N ₄ O ₄			91%	6.9	537.2



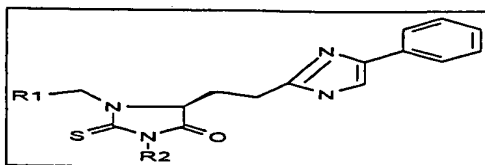
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
126	C30H30N4O3			90%	6.9	495.2
127	C27H23BrN4O3			89%	6.6	533.1
128	C27H23ClN4O3			91%	6.5	487.2
129	C27H23N5O5			75%	6.4	498.2
130	C33H36N4O3			90%	7.2	537.3
131	C27H22F2N4O3			82%	6.1	489.2
132	C30H30N4O6			79%	6.0	543.2
133	C28H23F3N4O3			90%	6.8	521.2
134	C29H26N4O4			85%	5.9	495.2
135	C28H26N4O3			89%	6.2	467.2
136	C29H28N4O3			89%	6.4	481.2
137	C24H26N4O3			88%	5.7	419.3
138	C25H28N4O3			90%	6.1	433.3
139	C24H24N4O3			92%	5.6	417.3
140	C26H30N4O3			87%	6.4	447.3



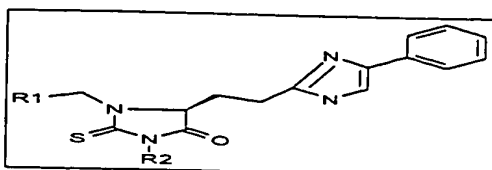
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
141	C ₂₈ H ₂₇ N ₅ O ₂			89%	5.1	466.2
142	C ₂₉ H ₂₉ N ₅ O ₂			89%	5.5	480.3
143	C ₂₉ H ₂₉ N ₅ O ₃			90%	5.2	496.3
144	C ₂₉ H ₂₉ N ₅ O ₂ S			86%	5.7	512.2
145	C ₂₉ H ₂₆ F ₃ N ₅ O ₃			87%	6.2	550.2
146	C ₃₁ H ₃₃ N ₅ O ₂			87%	6.2	508.3
147	C ₂₈ H ₂₆ BrN ₅ O ₂			88%	5.8	546.1
148	C ₂₈ H ₂₆ ClN ₅ O ₂			88%	5.7	500.2
149	C ₂₈ H ₂₆ N ₆ O ₄			74.76%*	5.6	511.2
150	C ₃₄ H ₃₉ N ₅ O ₂			85%	6.7	550.3
151	C ₂₈ H ₂₅ F ₂ N ₅ O ₂			81%	5.3	502.2
152	C ₃₁ H ₃₃ N ₅ O ₅			79%	5.2	556.3
153	C ₂₉ H ₂₆ F ₃ N ₅ O ₂			88%	6.1	534.2
154	C ₃₀ H ₂₉ N ₅ O ₃			85%	5.1	508.3
155	C ₂₉ H ₂₉ N ₅ O ₂			86%	5.4	480.3



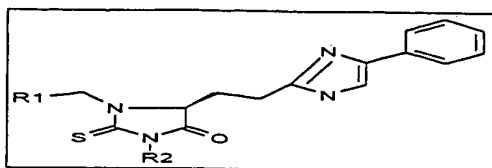
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
156	C ₃₀ H ₃₁ N ₅ O ₂			88%	5.6	494.3
157	C ₂₅ H ₂₉ N ₅ O ₂			85%	4.8	432.3
158	C ₂₆ H ₃₁ N ₅ O ₂			84%	5.2	446.3
159	C ₂₅ H ₂₇ N ₅ O ₂			86%	4.7	430.3
160	C ₂₇ H ₃₃ N ₅ O ₂			88%	5.6	460.3



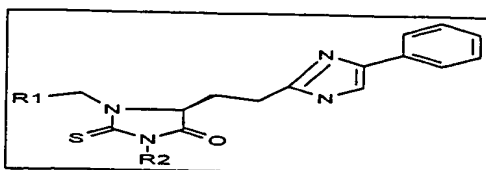
						Analyses
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
161	C ₃₀ H ₂₇ N ₅ O ₂ S			80%	7.1	506.2
162	C ₃₀ H ₂₆ ClN ₅ O ₂ S			83%	7.3	540.2
163	C ₃₀ H ₂₅ Cl ₂ N ₅ O ₂ S			81%	7.7	574.1
164	C ₃₁ H ₂₇ N ₅ O ₃ S			81%	7.0	550.2
165	C ₃₀ H ₂₆ FN ₅ O ₂ S			82%	7.1	524.3
166	C ₃₁ H ₂₉ N ₅ O ₂ S			81%	7.3	520.3
167	C ₃₁ H ₂₈ ClN ₅ O ₂ S			83%	7.6	554.2
168	C ₃₃ H ₃₃ N ₅ O ₃ S			80%	7.0	580.3
169	C ₃₂ H ₃₁ N ₅ O ₂ S			78%	7.4	534.3
170	C ₂₈ H ₂₅ N ₅ O ₂ S			85%	6.7	496.3
171	C ₂₈ H ₂₉ N ₅ O ₂ S			81%	6.6	500.3
172	C ₂₈ H ₂₉ N ₅ O ₂ S			71%	7.1	484.3
173	C ₂₉ H ₃₁ N ₅ O ₂ S			61%	7.3	498.3
174	C ₃₀ H ₃₃ N ₅ O ₂ S			64%	7.6	512.3
175	C ₂₉ H ₃₂ N ₆ O ₂ S			84%	5.0	529.3



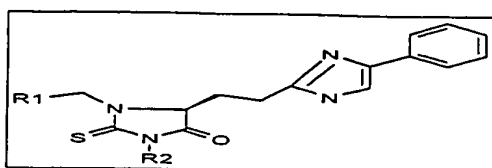
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
176	C30H34N6O2S			86%	5.0	543.3
177	C30H36N6OS			83%	5.2	529.3
178	C26H27N5O2S			82%	6.3	474.3
179	C27H29N5O2S			80%	6.4	488.3
180	C27H29N5OS			74%	7.0	472.3
181	C26H24N4OS2			77%	6.9	473.2
182	C26H23ClN4OS2			78%	7.1	507.2
183	C26H22Cl2N4OS2			84%	7.6	541.1
184	C27H24N4O3S2			80%	6.9	517.2
185	C26H23FN4OS2			75%	7.0	491.2
186	C27H26N4OS2			80%	7.1	487.2
187	C27H25ClN4OS2			85%	7.4	521.2
188	C29H30N4O3S2			87%	6.8	547.2
189	C28H28N4OS2			77%	7.3	501.2
190	C24H22N4O2S2			86%	6.5	463.2



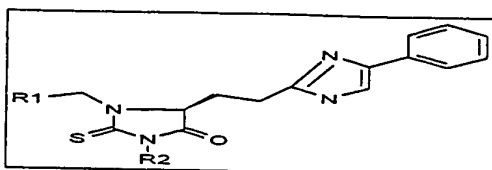
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
191	C24H26N4O2S2			58.9% +19.6%	6.4	467.2
192	C24H26N4OS2			75%	6.9	451.2
193	C25H28N4OS2			77%	7.2	465.2
194	C26H30N4OS2			76%	7.5	479.3
195	C25H29N5O2S2			81%	4.8	496.3
196	C26H31N5O2S2			82%	4.9	510.3
197	C26H33N5OS2			71%	5.0	496.3
198	C22H24N4O2S2			81%	6.1	441.2
199	C23H26N4O2S2			78%	6.2	455.2
200	C23H26N4OS2			79%	6.8	551.2
201	C29H28N4O2S			80%	7.0	497.3
202	C29H27ClN4O2S			81%	7.2	643.2
203	C29H26Cl2N4O2S			86%	7.6	677.2
204	C30H28N4O4S			82%	7.0	653.2
205	C29H27FN4O2S			72%	7.1	627.2



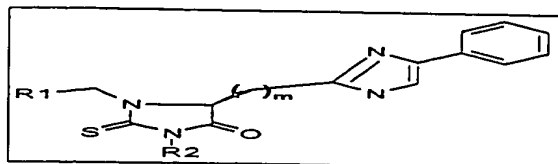
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
206	C30H30N4O2S			83%	7.2	511.3
207	C30H29CIN4O2S			87%	7.5	657.2
208	C32H34N4O4S			87%	6.9	571.3
209	C31H32N4O2S			83%	7.4	637.3
210	C27H26N4O3S			87%	6.6	599.2
211	C27H30N4O3S			59% +20%	6.5+6.6	491.2
212	C27H30N4O2S			81%	7.0	475.5
213	C28H32N4O2S			82%	7.2	601.2
214	C29H34N4O2S			83%	7.5	615.3
215	C28H33N5O3S			86%	5.0	520.3
216	C29H35N5O3S			86%	5.0	646.3
217	C29H37N5O2S			78%	5.1	632.3
218	C25H28N4O3S			87%	6.2	577.2
219	C26H30N4O3S			80%	6.4	591.3
220	C26H30N4O2S			85%	6.9	575.2



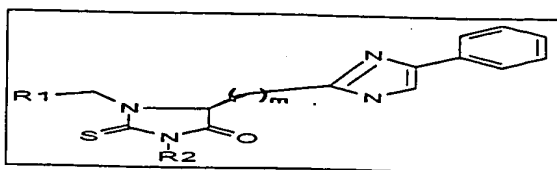
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
221	C30H31N5OS			77%	6.5	510.3
222	C30H30ClN5OS			66%	6.8	544.3
223	C30H29Cl2N5OS			69%	7.3	690.2
224	C31H31N5O3S			75%	6.4	666.3
225	C30H30FN5OS			52%	6.6	528.5
226	C31H33N5OS			82%	6.7	636.3
227	C31H32ClN5OS			85%	7.1	670.3
228	C33H37N5O3S			82%	6.4	696.3
229	C32H35N5OS			66%	7.0	650.3
230	C28H29N5O2S			77%	6.1	612.2
231	C28H33N5O2S			26%+48	5.8+5.9	616.3
232	C28H33N5OS			76%	6.4	600.3
233	C29H35N5OS			78%	6.7	614.3
234	C30H37N5OS			77%	4.6	645.3
235	C29H36N6O2S			85%	4.6	659.4



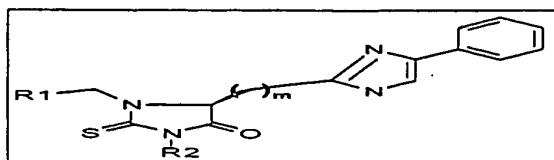
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
236	C ₃₀ H ₃₈ N ₆ O ₂ S			84%	4.8	532.3
237	C ₃₀ H ₄₀ N ₆ O ₂ S			36%	5.5	590.3
238	C ₂₆ H ₃₁ N ₅ O ₂ S			79%	5.7	492.3
239	C ₂₇ H ₃₃ N ₅ O ₂ S			69%	6.3	588.3
240	C ₂₇ H ₃₃ N ₅ O ₂ S			78%	6.3	476.3



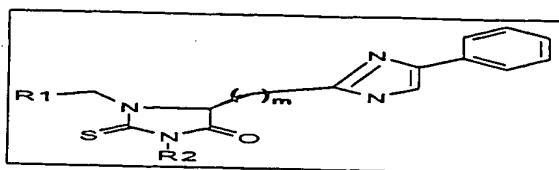
Analyses							
Ex. No.	Formula	m	R1	R2	Purity	rt (min)	[M+H] ⁺
241	C ₂₉ H ₂₅ N ₅ O ₂ S	2			93%	6.7	492.2
242	C ₃₁ H ₂₇ N ₅ O ₂ S	2			87%	6.6	534.2
243	C ₃₅ H ₃₇ N ₅ O ₂ S	2			68%	7.9	576.3
244	C ₃₂ H ₃₁ N ₅ O ₂ S	2			88%	7.5	534.2
245	C ₂₉ H ₂₃ F ₂ N ₅ O ₂ S	2			92%	6.9	528.2
246	C ₂₉ H ₂₄ FN ₅ O ₂ S	2			92%	6.8	510.2
247	C ₂₉ H ₂₂ Cl ₃ N ₅ O ₂ S	2			82%	7.6	594.1
248	C ₂₉ H ₂₃ Cl ₂ N ₅ O ₂ S	2			86%	7.5	560.1
249	C ₂₉ H ₂₂ Br ₃ N ₅ O ₂ S	2			76%	7.8	725.9
250	C ₃₁ H ₂₉ N ₅ O ₂ S	2			47%	7.1	520.2
251	C ₃₁ H ₂₃ F ₆ N ₅ O ₂ S	2			88%	7.8	628.2
252	C ₃₀ H ₂₄ F ₃ N ₅ O ₂ S	2			90%	7.3	560.2
253	C ₃₁ H ₂₉ N ₅ O ₃ S	2			86%	6.9	552.2
254	C ₃₀ H ₂₇ N ₅ O ₂ S	2			93%	6.8	522.2
255	C ₃₀ H ₂₇ N ₅ O ₂ S	2			88%	7.1	538.2



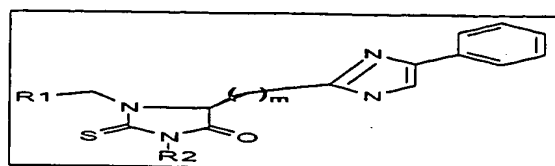
Ex. No.	Formula	m	R1	R2	Purity	rt (min)	[M+H] ⁺
256	C ₂₉ H ₂₄ N ₆ O ₃ S	2			92%	6.9	537.2
257	C ₂₉ H ₂₄ N ₈ O ₅ S	2			92%	7.1	533.2
258	C ₃₁ H ₃₀ N ₆ O ₅ S	2			67%	6.7	268.2
259	C ₃₀ H ₂₄ N ₆ O ₅ S	2			82%	6.7	517.2
260	C ₃₆ H ₃₁ N ₅ O ₂ S	2			86%	7.6	598.2
261	C ₂₉ H ₂₉ N ₅ O ₅ S	2			78%	6.1	248.7
262	C ₃₁ H ₃₁ N ₅ O ₂ S	2			65%	6.0	269.7
263	C ₃₅ H ₄₁ N ₅ O ₅ S	2			53%	7.5	290.8
264	C ₃₂ H ₃₅ N ₅ O ₅ S	2			82%	7.0	269.8
265	C ₂₉ H ₂₇ F ₂ N ₅ O ₅ S	2			79%	6.4	266.7
266	C ₂₉ H ₂₈ FN ₅ O ₅ S	2			73%	6.2	257.7
267	C ₂₉ H ₂₆ Cl ₃ N ₅ O ₅ S	2			87%	7.2	299.6
268	C ₂₉ H ₂₇ Cl ₂ N ₅ O ₅ S	2			70%	7.1	282.6
269	C ₂₉ H ₂₆ Br ₃ N ₅ O ₅ S	2			78%	7.3	365.5
270	C ₃₁ H ₃₃ N ₅ O ₅ S	2			3%	6.6	262.7



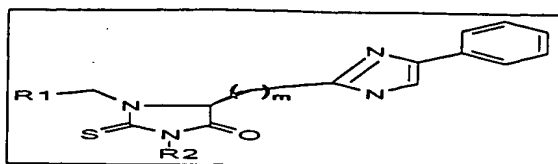
Ex. No.	Formula	m	R1	R2	Purity	rt (min)	[M+H] ⁺
271	C31H27F6N5OS	2			39%	7.5	316.8
272	C30H28F3N5OS	2			64%	6.9	282.7
273	C31H33N5O3S	2			78%	6.3	278.7
274	C30H31N5O2S	2			45%	6.2	263.7
275	C30H31N5OS2	2			66%	6.5	271.7
276	C29H28N6O3S	2			67%	6.4	271.2
277	C29H28N8OS	2			62%	6.5	269.2
278	C31H34N6OS	2			37%	6.1	270.2
279	C30H28N6OS	2			49%	6.1	261.3
280	C36H35N5O2S	2			73%	7.2	301.8
281	C24H20N4OS2	1			89%	6.6	445.1
282	C26H22N4O2S2	1			88%	6.6	487.2
283	C30H32N4OS2	1			86%	7.9	529.2
284	C27H26N4OS2	1			96%	7.5	487.2
285	C24H18F2N4OS2	1			93%	6.7	481.1



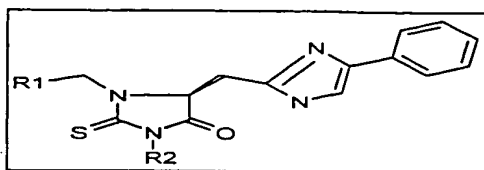
Ex. No.	Formula	m	R1	R2	Purity	rt (min)	[M+H] ⁺
286	C ₂₄ H ₁₉ FN ₄ OS ₂	1			90%	6.8	463.1
287	C ₂₄ H ₁₇ Cl ₃ N ₄ OS ₂	1			97%	7.5	547.0
288	C ₂₄ H ₁₈ Cl ₂ N ₄ OS ₂	1			90%	7.8	513.1
289	C ₂₄ H ₁₇ Br ₃ N ₄ OS ₂	1			92%	7.7	678.9
290	C ₂₆ H ₂₄ N ₄ OS ₂	1			87%	7.0	473.2
291	C ₂₆ H ₁₈ F ₆ N ₄ OS ₂	1			91%	8.2	581.1
292	C ₂₅ H ₁₉ F ₃ N ₄ OS ₂	1			87%	7.5	513.1
293	C ₂₆ H ₂₄ N ₄ O ₃ S ₂	1			95%	6.8	505.2
294	C ₂₅ H ₂₂ N ₄ O ₂ S ₂	1			92%	6.7	475.1
295	C ₂₅ H ₂₂ N ₄ OS ₃	1			89%	7.1	491.1
296	C ₂₄ H ₁₉ N ₅ O ₃ S ₂	1			88%	7.0	490.1
297	C ₂₄ H ₁₉ N ₇ OS ₂	1			90%	7.1	486.2
298	C ₂₆ H ₂₅ N ₅ OS ₂	1			86%	6.6	244.7
299	C ₂₅ H ₁₉ N ₅ OS ₂	1			89%	6.8	470.1
300	C ₃₁ H ₂₆ N ₄ O ₂ S ₂	1			88%	7.7	551.2



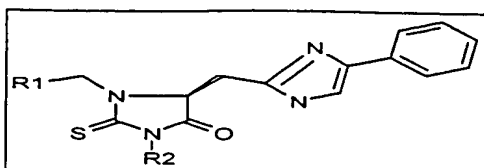
Ex. No.	Formula	m	R1	R2	Purity	rt (min)	[M+H] ⁺
301	C ₂₇ H ₂₄ N ₄ O ₂ S	1			92%	6.7	469.2
302	C ₂₉ H ₂₆ N ₄ O ₃ S	1			91%	6.7	511.2
303	C ₃₃ H ₃₆ N ₄ O ₂ S	1			89%	8.0	553.3
304	C ₃₀ H ₃₀ N ₄ O ₂ S	1			95%	7.6	511.2
305	C ₂₇ H ₂₂ F ₂ N ₄ O ₂ S	1			95%	6.8	505.2
306	C ₂₇ H ₂₃ FN ₄ O ₂ S	1			93%	6.9	487.2
307	C ₂₇ H ₂₁ Cl ₃ N ₄ O ₂ S	1			93%	7.6	571.1
308	C ₂₇ H ₂₂ Cl ₂ N ₄ O ₂ S	1			85%	7.9	537.1
309	C ₂₇ H ₂₁ Br ₃ N ₄ O ₂ S	1			93%	7.8	702.9
310	C ₂₉ H ₂₈ N ₄ O ₂ S	1			86%	7.1	497.2
311	C ₂₉ H ₂₂ F ₆ N ₄ O ₂ S	1			93%	8.3	605.2
312	C ₂₈ H ₂₃ F ₃ N ₄ O ₂ S	1			93%	7.5	537.1
313	C ₂₉ H ₂₈ N ₄ O ₄ S	1			96%	6.9	529.2
314	C ₂₈ H ₂₆ N ₄ O ₃ S	1			97%	6.8	499.2
315	C ₂₈ H ₂₆ N ₄ O ₂ S ₂	1			84%	7.2	515.2



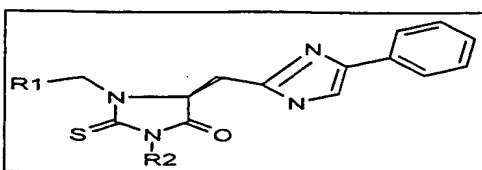
Ex. No.	Formula	m	R1	R2	Purity	rt (min)	[M+H] ⁺
316	C ₂₇ H ₂₃ N ₅ O ₄ S	1			88%	7.1	514.2
317	C ₂₇ H ₂₃ N ₇ O ₂ S	1			94%	7.2	510.2
318	C ₂₉ H ₂₉ N ₅ O ₂ S	1			89%	6.7	256.7
319	C ₂₈ H ₂₃ N ₅ O ₂ S	1			90%	6.8	494.2
320	C ₃₄ H ₃₀ N ₄ O ₃ S	1			89%	7.7	575.2



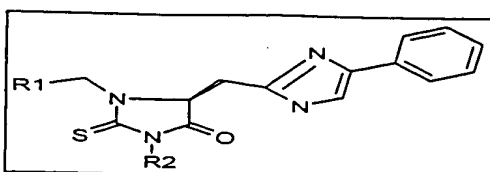
						Analyses	
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺	
321	C ₂₉ H ₂₅ N ₅ O ₃ S			91	7.2	492.2	
322	C ₂₉ H ₂₄ ClN ₅ O ₃ S			91	7.5	526.2	
323	C ₂₉ H ₂₃ Cl ₂ N ₅ O ₃ S			91	7.9	560.1	
324	C ₃₀ H ₂₅ N ₅ O ₃ S			92	7.0	536.2	
325	C ₂₉ H ₂₄ FN ₅ O ₃ S			93	7.3	510.2	
326	C ₃₀ H ₂₇ N ₅ O ₃ S			92	7.4	506.2	
327	C ₃₀ H ₂₆ ClN ₅ O ₃ S			91	7.8	540.2	
328	C ₃₂ H ₃₁ N ₅ O ₃ S			90	7.1	566.2	
329	C ₃₁ H ₂₉ N ₅ O ₃ S			91	7.6	520.2	
330	C ₂₇ H ₂₃ N ₅ O ₂ S			92	6.8	482.2	
331	C ₂₇ H ₂₇ N ₅ O ₂ S			35+51	6.64+6.76	486.2	
332	C ₂₇ H ₂₇ N ₅ O ₃ S			90	7.2	470.2	
333	C ₂₈ H ₂₉ N ₅ O ₃ S			89	7.4	484.3	
334	C ₂₉ H ₃₁ N ₅ O ₃ S			90	7.7	498.3	
335	C ₂₈ H ₃₀ N ₆ O ₂ S			94	5.2	258.3	
336	C ₂₉ H ₃₂ N ₆ O ₂ S			93	5.1	265.3	



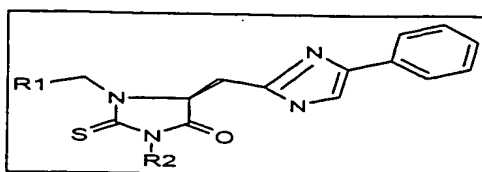
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
337	C ₂₉ H ₃₄ N ₆ O ₂ S			85	5.3	258.3
338	C ₂₅ H ₂₅ N ₅ O ₂ S			92	6.4	460.2
339	C ₂₆ H ₂₇ N ₅ O ₂ S			92	6.5	474.2
340	C ₂₆ H ₂₇ N ₅ O ₂ S			91	7.1	458.2
341	C ₂₅ H ₂₂ N ₄ O ₂ S			90	7.0	459.2
342	C ₂₅ H ₂₁ ClN ₄ O ₂ S			89	7.4	493.1
343	C ₂₅ H ₂₀ Cl ₂ N ₄ O ₂ S			92	7.7	527.1
344	C ₂₆ H ₂₂ N ₄ O ₃ S ₂			88	6.9	503.2
345	C ₂₅ H ₂₁ FN ₄ O ₂ S			91	7.1	477.2
346	C ₂₆ H ₂₄ N ₄ O ₂ S			89	7.3	473.2
347	C ₂₆ H ₂₃ ClN ₄ O ₂ S			91	7.7	507.1
348	C ₂₈ H ₂₈ N ₄ O ₃ S ₂			88	6.9	533.2
349	C ₂₇ H ₂₆ N ₄ O ₂ S			85	7.5	487.2
350	C ₂₃ H ₂₀ N ₄ O ₂ S ₂			93	6.6	449.1
351	C ₂₃ H ₂₄ N ₄ O ₂ S ₂			36+50	6.34+6.46	453.2
352	C ₂₃ H ₂₄ N ₄ O ₂ S			87	7.0	437.2



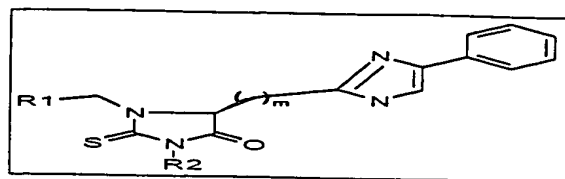
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
353	C24H26N4OS2			84	7.3	451.2
354	C25H28N4OS2			86	7.5	465.2
355	C24H27N5O2S2			91	5.0	241.7
356	C25H29N5O2S2			88	5.0	248.8
357	C25H31N5OS2			61	5.1	241.8
358	C21H22N4O2S2			88	6.1	427.1
359	C22H24N4O2S2			87	6.3	441.1
360	C22H24N4OS2			84	6.9	425.2
361	C28H26N4O2S			89	7.1	483.2
362	C28H25ClN4O2S			89	7.5	517.2
363	C28H24Cl2N4O2S			91	7.8	551.1
364	C29H26N4O4S			89	7.0	527.2
365	C28H25FN4O2S			95	7.2	501.2
366	C29H28N4O2S			90	7.3	497.2
367	C29H27ClN4O2S			89	7.7	531.2
368	C31H32N4O4S			90	7.0	557.2



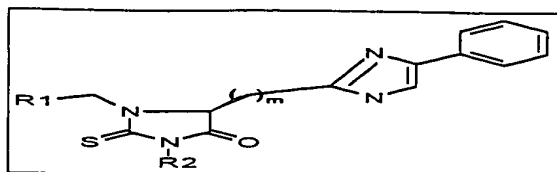
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
369	C30H30N4O2S			91	7.5	511.2
370	C26H24N4O3S			92	6.7	473.2
371	C26H28N4O3S			39+45	6.44+6.56	477.2
372	C26H28N4O2S			89	7.1	461.2
373	C27H30N4O2S			90	7.3	475.2
374	C28H32N4O2S			90	7.6	489.3
375	C27H31N5O3S			93	5.1	253.7
376	C28H33N5O3S			90	5.1	260.8
377	C28H35N5O2S			73	5.3	253.8
378	C24H26N4O3S			91	6.2	451.2
379	C25H28N4O3S			91	6.4	465.2
380	C25H28N4O2S			90	7.0	449.2
381	C29H29N5OS			85	6.4	248.7
382	C29H28ClN5OS			85	6.9	265.7
383	C29H27Cl2N5OS			84	7.3	282.6
384	C30H29N5O3S			85	6.3	270.7



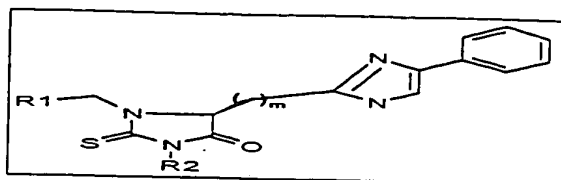
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
385	C ₂₉ H ₂₈ N ₅ O ₂ S			88	6.5	257.7
386	C ₃₀ H ₃₁ N ₅ O ₂ S			84	6.7	255.6
387	C ₃₀ H ₃₀ CIN ₅ O ₂ S			87	7.2	272.7
388	C ₃₂ H ₃₅ N ₅ O ₃ S			82	6.4	285.8
389	C ₃₁ H ₃₃ N ₅ O ₂ S			81	6.9	262.7
390	C ₂₇ H ₂₇ N ₅ O ₂ S			89	5.9	243.7
391	C ₂₇ H ₃₁ N ₅ O ₂ S			43+43	5.68+5.86	245.7
392	C ₂₇ H ₃₁ N ₅ O ₂ S			83	6.4	237.7
393	C ₂₈ H ₃₃ N ₅ O ₂ S			83	6.7	244.7
394	C ₂₉ H ₃₅ N ₅ O ₂ S			85	7.0	251.7
395	C ₂₈ H ₃₄ N ₆ O ₂ S			87	4.6	259.8
396	C ₂₉ H ₃₆ N ₆ O ₂ S			84	4.6	267.2
397	C ₂₅ H ₂₉ N ₅ O ₂ S			74	5.4	232.7
398	C ₂₆ H ₃₁ N ₅ O ₂ S			83	5.6	239.7
399	C ₂₆ H ₃₁ N ₅ O ₂ S			87	6.3	231.8



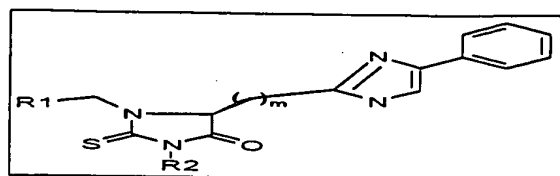
						Analyses	
Ex. No.	Formula	m	R1	R2	Purity	rt (min)	[M+H] ⁺
400	C30H34N6O3S	2			83%	7.8	559.2
401	C31H36N6O3S	2			82%	7.9	573.2
402	C32H38N6O3S	2			82%	8.0	587.3
403	C33H40N6O3S	2			81%	8.3	601.3
404	C34H42N6O3S	2			80%	8.5	615.3
405	C26H31N5O3S2	2			81%	7.6	526.2
406	C27H33N5O3S2	2			83%	7.8	540.2
407	C28H35N5O3S2	2			88%	7.9	554.2
408	C29H37N5O3S2	2			86%	8.2	568.2
409	C30H39N5O3S2	2			86%	8.4	582.3
410	C29H35N5O4S	2			87%	7.7	550.3
411	C30H37N5O4S	2			87%	7.9	564.3
412	C31H39N5O4S	2			92%	8.0	578.3
413	C32H41N5O4S	2			89%	8.3	592.3
414	C33H43N5O4S	2			88%	8.5	606.3



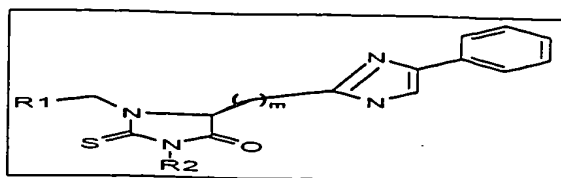
Ex. No.	Formula	m	R1	R2	Purity	rt (min)	[M+H] ⁺
415	C30H38N6O3S	2			83%	7.0	563.3
416	C31H40N6O3S	2			85%	7.2	577.3
417	C32H42N6O3S	2			88%	7.4	591.3
418	C33H44N6O3S	2			88%	7.7	303.3
419	C34H46N6O3S	2			88%	7.9	310.4
420	C29H32N6O3S	2			78%	7.9	545.2
421	C30H34N6O3S	2			81%	8.0	559.2
422	C31H36N6O3S	2			84%	8.1	573.3
423	C32H38N6O3S	2			82%	8.3	587.3
424	C33H40N6O3S	2			86%	8.5	601.3
425	C25H29N5O3S2	2			80%	7.7	512.2
426	C26H31N5O3S2	2			82%	7.8	526.2
427	C27H33N5O3S2	2			87%	7.9	540.2
428	C28H35N5O3S2	2			86%	8.2	554.2
429	C29H37N5O3S2	2			84%	8.4	568.2



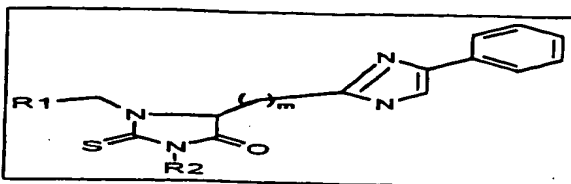
Ex. No.	Formula	m	R1	R2	Purity	rt (min)	[M+H] ⁺
430	C ₂₈ H ₃₃ N ₅ O ₄ S	2			86%	7.8	536.3
431	C ₂₉ H ₃₅ N ₅ O ₄ S	2			85%	7.9	550.3
432	C ₃₀ H ₃₇ N ₅ O ₄ S	2			92%	8.0	564.3
433	C ₃₁ H ₃₉ N ₅ O ₄ S	2			90%	8.2	578.3
434	C ₃₂ H ₄₁ N ₅ O ₄ S	2			90%	8.5	592.3
435	C ₂₉ H ₃₆ N ₆ O ₃ S	2			80%	6.9	549.3
436	C ₃₀ H ₃₈ N ₆ O ₃ S	2			78%	7.1	563.3
437	C ₃₁ H ₄₀ N ₆ O ₃ S	2			84%	7.3	577.3
438	C ₃₂ H ₄₂ N ₆ O ₃ S	2			83%	7.5	296.3
439	C ₃₃ H ₄₄ N ₆ O ₃ S	2			85%	7.8	303.3
440	C ₂₅ H ₂₆ N ₆ O ₃ S	1			76%	5.4	459.2
441	C ₂₆ H ₂₈ N ₆ O ₃ S	1			61%	5.4	473.3
442	C ₂₇ H ₃₀ N ₆ O ₃ S	1			75%	5.6	244.2
443	C ₂₈ H ₃₂ N ₆ O ₃ S	1			32%	5.7	251.1
444	C ₂₉ H ₃₄ N ₆ O ₃ S	1			59%	5.9	258.3



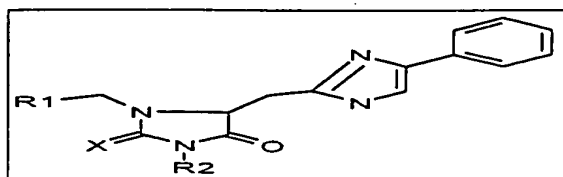
Ex. No.	Formula	m	R1	R2	Purity	rt (min)	[M+H] ⁺
445	C21H23N5OS2	1			78%	5.1	426.2
446	C22H25N5OS2	1			79%	5.2	440.2
447	C23H27N5OS2	1			84%	5.4	227.6
448	C24H29N5OS2	1			84%	5.5	234.7
449	C25H31N5OS2	1			83%	5.7	241.7
450	C24H27N5O2S	1			88%	5.3	450.2
451	C25H29N5O2S	1			96%	5.4	464.2
452	C26H31N5O2S	1			90%	5.6	239.7
453	C27H33N5O2S	1			90%	5.7	246.7
454	C28H35N5O2S	1			91%	5.9	253.7
455	C25H30N6OS	1			84%	4.8	232.2
456	C26H32N6OS	1			89%	4.9	238.8
457	C27H34N6OS	1			86%	5.0	246.1
458	C28H36N6OS	1			93%	5.2	252.9
459	C29H38N6OS	1			93%	5.4	260.1



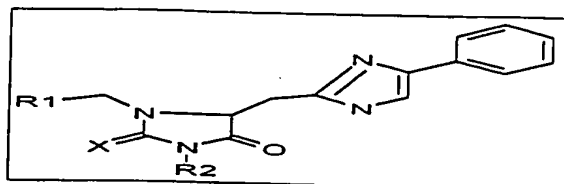
Ex. No.	Formula	m	R1	R2	Purity	rt (min)	[M+H] ⁺
460	C ₂₄ H ₂₄ N ₆ O ₂ S	1			68%	5.6	445.2
461	C ₂₅ H ₂₆ N ₆ O ₂ S	1			55%	5.5	459.2
462	C ₂₆ H ₂₈ N ₆ O ₂ S	1			55%	5.6	473.3
463	C ₂₇ H ₃₀ N ₆ O ₂ S	1			48%	5.7	487.3
464	C ₂₈ H ₃₂ N ₆ O ₂ S	1			44%	5.9	501.2
465	C ₂₀ H ₂₁ N ₅ O ₂ S ₂	1			84%	5.3	412.1
466	C ₂₁ H ₂₃ N ₅ O ₂ S ₂	1			86%	5.2	426.2
467	C ₂₂ H ₂₅ N ₅ O ₂ S ₂	1			90%	5.3	440.2
468	C ₂₃ H ₂₇ N ₅ O ₂ S ₂	1			79%	5.5	227.7
469	C ₂₄ H ₂₉ N ₅ O ₂ S ₂	1			91%	5.7	234.8
470	C ₂₃ H ₂₅ N ₅ O ₂ S ₂	1			92%	5.5	436.2
471	C ₂₄ H ₂₇ N ₅ O ₂ S ₂	1			88%	5.4	450.2
472	C ₂₅ H ₂₉ N ₅ O ₂ S ₂	1			93%	5.5	464.3
473	C ₂₆ H ₃₁ N ₅ O ₂ S ₂	1			92%	5.6	478.3
474	C ₂₇ H ₃₃ N ₅ O ₂ S ₂	1			95%	5.8	246.7



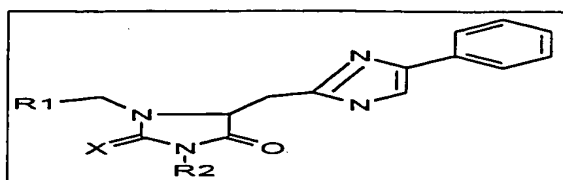
Ex. No.	Formula	m	R1	R2	Purity	rt (min)	[M+H] ⁺
475	C ₂₄ H ₂₈ N ₆ O ₅	1			87%	4.9	224.7
476	C ₂₅ H ₃₀ N ₆ O ₅	1			80%	4.8	231.9
477	C ₂₆ H ₃₂ N ₆ O ₅	1			84%	4.9	238.9
478	C ₂₇ H ₃₄ N ₆ O ₅	1			90%	5.0	245.7
479	C ₂₈ H ₃₆ N ₆ O ₅	1			91%	5.2	505.3



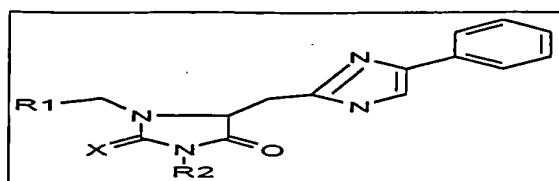
							Analyses	
Ex. No.	Formula	X	R1	R2	Purity	rt (min)	[M+H] ⁺	
480	C30H34N6O3S	S			86%	5.4	559.2	
481	C31H36N6O3S	S			88%	5.5	573.2	
482	C32H38N6O3S	S			88%	5.5	587.3	
483	C33H40N6O3S	S			89%	5.7	601.3	
484	C34H42N6O3S	S			91%	5.8	615.3	
485	C35H36N6O3S	S			91%	5.6	621.3	
486	C31H34N6O4S	S			56%	5.6	587.2	
487	C32H36N6O4S	S			73%	5.6	601.2	
488	C33H38N6O4S	S			79%	5.7	615.3	
489	C34H40N6O4S	S			71%	5.9	629.3	
490	C35H42N6O4S	S			81%	6.0	643.3	
491	C36H36N6O4S	S			60%	5.8	649.3	
492	C30H34N6O3S	S			83%	5.4	559.2	
493	C31H36N6O3S	S			87%	5.5	573.2	
494	C32H38N6O3S	S			87%	5.5	587.3	



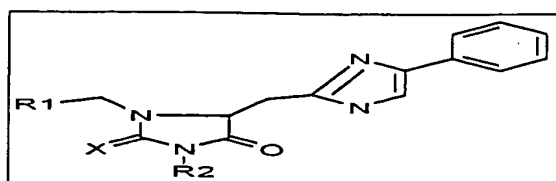
Ex. No.	Formula	X	R1	R2	Purity	rt (min)	[M+H] ⁺
495	C33H40N6O3S	S			87%	5.7	601.3
496	C34H42N6O3S	S			88%	5.8	615.3
497	C35H36N6O3S	S			89%	5.6	621.3
498	C31H34N6O4S	S			71%	5.6	587.2
499	C32H36N6O4S	S			45%	5.6	601.2
500	C33H38N6O4S	S			75%	5.7	615.3
501	C34H40N6O4S	S			68%	5.9	629.3
502	C35H42N6O4S	S			76%	6.0	643.3
503	C36H36N6O4S	S			55%	5.8	649.3
504	C30H34N6O4	O			88%	4.9	543.3
505	C31H36N6O4	O			88%	5.0	557.3
506	C32H38N6O4	O			85%	5.0	571.3
507	C33H40N6O4	O			86%	5.2	585.3
508	C31H34N6O5	O			79%	4.9	571.2
509	C32H36N6O5	O			56%	5.0	585.3



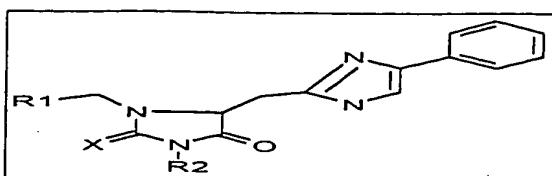
Ex. No.	Formula	X	R1	R2	Purity	rt (min)	[M+H] ⁺
510	C33H38N6O5	O			77%	5.1	599.3
511	C34H40N6O5	O			74%	5.2	613.3
512	C30H34N6O4	O			90%	4.9	543.3
513	C31H36N6O4	O			90%	5.0	557.3
514	C32H38N6O4	O			89%	5.0	571.3
515	C33H40N6O4	O			91%	5.2	585.3
516	C31H34N6O5	O			76%	4.9	571.2
517	C32H36N6O5	O			81%	5.0	585.3
518	C33H38N6O5	O			74%	5.1	599.3
519	C34H40N6O5	O			75%	5.2	613.3
520	C25H26N6OS	S			93%	6.8	459.2
521	C26H28N6OS	S			93%	6.6	473.2
522	C27H30N6OS	S			90%	6.7	487.2
523	C28H32N6OS	S			92%	6.8	501.2
524	C29H34N6OS	S			92%	6.9	515.2



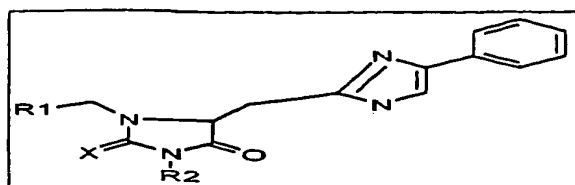
Ex. No.	Formula	X	R1	R2	Purity	rt (min)	[M+H] ⁺
525	C30H28N6OS	S			89%	6.8	521.2
526	C26H26N6O2S	S			63%	7.1	487.2
527	C27H28N6O2S	S			87%	6.8	501.2
528	C28H30N6O2S	S			85%	6.9	515.2
529	C29H32N6O2S	S			79%	7.0	529.2
530	C30H34N6O2S	S			91%	7.2	543.2
531	C31H28N6O2S	S			80%	7.1	549.2
532	C25H26N6OS	S			91%	6.8	459.2
533	C26H28N6OS	S			89%	6.6	473.2
534	C27H30N6OS	S			93%	6.7	487.2
535	C28H32N6OS	S			91%	6.8	501.2
536	C29H34N6OS	S			91%	6.9	515.2
537	C30H28N6OS	S			87%	6.8	521.2
538	C26H26N6O2S	S			90%	7.0	487.2
539	C27H28N6O2S	S			61%	6.8	501.2



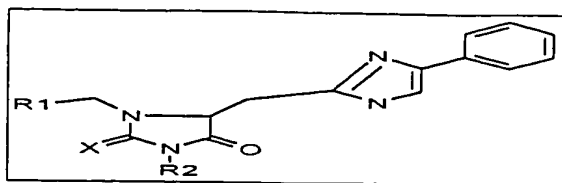
Ex. No.	Formula	X	R1	R2	Purity	rt (min)	[M+H] ⁺
540	C28H30N6O2S	S			87%	6.9	515.2
541	C29H32N6O2S	S			83%	7.0	529.2
542	C30H34N6O2S	S			93%	7.2	543.2
543	C31H28N6O2S	S			76%	7.1	549.2
544	C25H26N6O2	O			91%	6.1	443.2
545	C26H28N6O2	O			90%	6.1	457.2
546	C27H30N6O2	O			87%	6.1	471.2
547	C28H32N6O2	O			88%	6.2	485.2
548	C26H26N6O3	O			93%	6.2	471.2
549	C27H28N6O3	O			91%	6.1	485.2
550	C28H30N6O3	O			81%	6.2	499.2
551	C29H32N6O3	O			82%	6.3	513.2
552	C25H26N6O2	O			91%	6.1	443.2
553	C26H28N6O2	O			91%	6.1	457.2
554	C27H30N6O2	O			89%	6.1	471.2



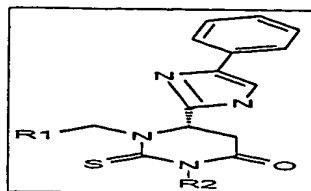
Ex. No.	Formula	X	R1	R2	Purity	rt (min)	[M+H] ⁺
555	C ₂₈ H ₃₂ N ₆ O ₂	O			91%	6.1	485.2
556	C ₂₆ H ₂₆ N ₆ O ₃	O			93%	6.2	471.2
557	C ₂₇ H ₂₈ N ₆ O ₃	O			95%	6.1	485.2
558	C ₂₈ H ₃₀ N ₆ O ₃	O			85%	6.2	499.2
559	C ₂₉ H ₃₂ N ₆ O ₃	O			85%	6.3	513.2



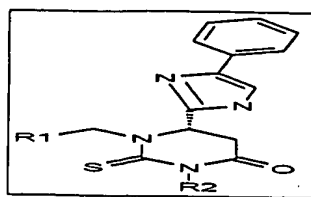
							Analyses	
Ex. No.	Formula	X	R1	R2	Purity	rt (min)	[M+H] ⁺	
560	C ₂₄ H ₂₄ N ₆ OS	S			84%	3.6	445.2	
561	C ₂₆ H ₂₈ N ₆ OS	S			92%	3.5	473.3	
562	C ₂₇ H ₃₀ N ₆ OS	S			83%	3.6	487.3	
563	C ₂₈ H ₃₂ N ₆ OS	S			88%	3.7	501.3	
564	C ₂₉ H ₂₆ N ₆ OS	S			59%	3.7	507.2	
565	C ₂₄ H ₂₄ N ₆ O ₂	O			87%	3.2	429.2	
566	C ₂₅ H ₂₆ N ₆ O ₂	O			92%	3.1	443.3	
567	C ₂₆ H ₂₈ N ₆ O ₂	O			97%	3.1	457.3	
568	C ₂₇ H ₃₀ N ₆ O ₂	O			90%	3.1	471.3	
569	C ₂₄ H ₂₄ N ₆ O ₂	O			91%	3.1	429.2	
570	C ₂₅ H ₂₆ N ₆ O ₂	O			97%	3.1	443.3	



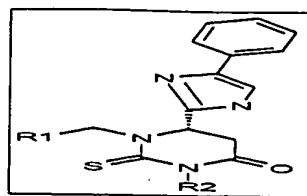
Ex. No.	Formula	X	R1	R2	Purity	rt (min)	[M+H] ⁺
571	C ₂₆ H ₂₈ N ₆ O ₂	O			95%	3.1	457.3
572	C ₂₇ H ₃₀ N ₆ O ₂	O			95%	3.2	471.3



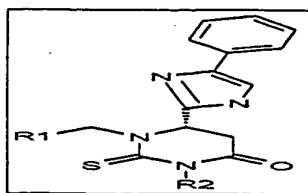
						Analyses
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
573	C ₂₉ H ₂₅ N ₅ O ₂ S			93%	6.7	492.2
574	C ₂₉ H ₂₄ ClN ₅ O ₂ S			93%	7.2	526.2
575	C ₂₉ H ₂₃ Cl ₂ N ₅ O ₂ S			93%	7.6	560.1
576	C ₃₀ H ₂₇ N ₅ O ₂ S			94%	7.0	506.2
577	C ₂₉ H ₂₄ FN ₅ O ₂ S			95%	6.9	510.3
578	C ₃₀ H ₂₇ N ₅ O ₂ S			90%	6.9	506.3
579	C ₃₀ H ₂₆ ClN ₅ O ₂ S			92%	7.4	540.2
580	C ₃₂ H ₃₁ N ₅ O ₃ S			88%	6.4	566.3
581	C ₃₁ H ₂₉ N ₅ O ₂ S			87%	7.1	520.2
582	C ₂₇ H ₂₃ N ₅ O ₂ S			93%	6.2	482.2
583	C ₂₇ H ₂₇ N ₅ O ₂ S			38+45%	5.6+5.71	486.3
584	C ₂₈ H ₃₀ N ₆ O ₂ S			87%	4.6	515.3
585	C ₂₉ H ₃₂ N ₆ O ₂ S			84%	4.5	529.3
586	C ₂₉ H ₃₄ N ₆ O ₂ S			89%	4.7	515.3
587	C ₂₅ H ₂₅ N ₅ O ₂ S			90%	5.18m	460.3



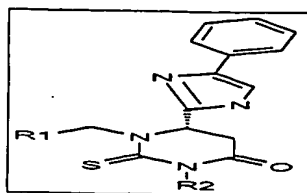
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
588	C ₂₆ H ₂₇ N ₅ O ₂ S			87%	5.6	474.3
589	C ₂₅ H ₂₂ N ₄ O ₂ S			89%	6.7	459.2
590	C ₂₅ H ₂₁ ClN ₄ O ₂ S			87%	7.2	493.2
591	C ₂₅ H ₂₀ Cl ₂ N ₄ O ₂ S			90%	7.6	527.1
592	C ₂₆ H ₂₄ N ₄ O ₂ S			83%	7.0	473.2
593	C ₂₅ H ₂₁ FN ₄ O ₂ S			88%	6.9	477.2
594	C ₂₆ H ₂₄ N ₄ O ₂ S			80%	7.0	473.2
595	C ₂₆ H ₂₃ ClN ₄ O ₂ S			79%	7.4	507.2
596	C ₂₈ H ₂₈ N ₄ O ₃ S ₂			82%	6.4	533.2
597	C ₂₇ H ₂₆ N ₄ O ₂ S			79%	7.2	487.2
598	C ₂₃ H ₂₀ N ₄ O ₂ S ₂			80%	6.2	449.2
599	C ₂₃ H ₂₄ N ₄ O ₂ S ₂			31+32%	5.7+5.86	453.2
600	C ₂₄ H ₂₇ N ₅ O ₂ S ₂			80%	4.3	241.7
601	C ₂₅ H ₂₉ N ₅ O ₂ S ₂			81%	4.3	248.8
602	C ₂₅ H ₃₁ N ₅ O ₂ S			81%	4.5	482.3



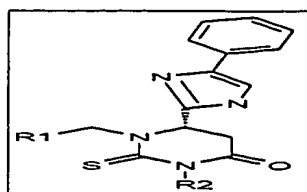
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
603	C21H22N4O2S2			79%	5.6	427.1
604	C22H24N4O2S2			78%	5.9	441.2
605	C28H26N4O2S			89%	6.8	483.2
606	C28H25ClN4O2S			90%	7.2	517.2
607	C28H24Cl2N4O2S			91%	7.7	551.1
608	C29H28N4O2S			88%	7.0	497.3
609	C28H25FN4O2S			89%	6.9	501.2
610	C29H28N4O2S			87%	7.0	497.3
611	C29H27ClN4O2S			90%	7.5	531.2
612	C31H32N4O4S			91%	6.5	557.2
613	C30H30N4O2S			87%	7.2	511.3
614	C26H24N4O3S			89%	6.3	473.2
615	C26H28N4O3S			39+43%	5.7+5.85	477.2
616	C27H31N5O3S			34%	4.5	506.3
617	C28H33N5O3S			79%	4.4	520.3



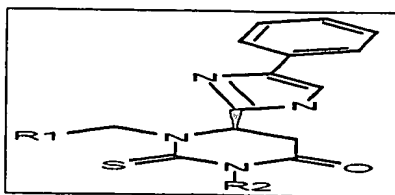
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
618	C ₂₈ H ₃₅ N ₅ O ₂ S			76%	4.6	506.3
619	C ₂₄ H ₂₆ N ₄ O ₃ S			85%	5.7	451.2
620	C ₂₅ H ₂₈ N ₄ O ₃ S			84%	5.9	465.2
621	C ₂₉ H ₂₉ N ₅ O ₂ S			89%	5.9	248.8
622	C ₂₉ H ₂₈ ClN ₅ O ₂ S			89%	6.4	265.7
623	C ₂₉ H ₂₇ Cl ₂ N ₅ O ₂ S			93%	6.9	282.7
624	C ₃₀ H ₃₁ N ₅ O ₂ S			90%	6.2	255.8
625	C ₂₉ H ₂₈ FN ₅ O ₂ S			92%	6.1	257.8
626	C ₃₀ H ₃₁ N ₅ O ₂ S			87%	6.2	255.8
627	C ₃₀ H ₃₀ ClN ₅ O ₂ S			90%	6.8	272.7
628	C ₃₂ H ₃₅ N ₅ O ₃ S			87%	5.6	285.8
629	C ₃₁ H ₃₃ N ₅ O ₂ S			88%	6.4	262.8
630	C ₂₇ H ₂₇ N ₅ O ₂ S			89%	5.4	243.7
631	C ₂₇ H ₃₁ N ₅ O ₂ S			31+37%	5.26+5.33	245.6
632	C ₂₈ H ₃₄ N ₆ O ₂ S			79%	3.7	260.3



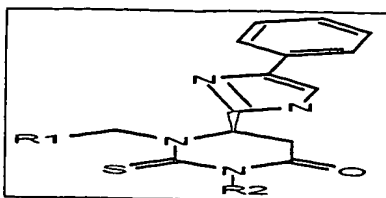
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
633	C ₂₉ H ₃₆ N ₆ O ₂ S			77%	3.7	267.3
634	C ₂₉ H ₃₈ N ₆ O ₂ S			78%	3.9	260.2
635	C ₂₅ H ₂₉ N ₅ O ₂ S			80%	4.9	232.7
636	C ₂₆ H ₃₁ N ₅ O ₂ S			79%	5.0	239.7
637	C ₂₈ H ₂₃ F ₃ N ₄ O ₂ S			88%	7.4	537.2
638	C ₂₈ H ₂₂ ClF ₃ N ₄ O ₂ S			90%	7.8	571.1
639	C ₂₈ H ₂₁ Cl ₂ F ₃ N ₄ O ₂ S			92%	8.3	605.1
640	C ₂₉ H ₂₅ F ₃ N ₄ O ₂ S			89%	7.6	551.2
641	C ₂₈ H ₂₂ F ₄ N ₄ O ₂ S			89%	7.5	555.2
642	C ₂₉ H ₂₅ F ₃ N ₄ O ₂ S			88%	7.7	551.2
643	C ₂₉ H ₂₄ ClF ₃ N ₄ O ₂ S			90%	8.1	585.1
644	C ₃₁ H ₂₉ F ₃ N ₄ O ₄ S			92%	7.2	611.2
645	C ₃₀ H ₂₇ F ₃ N ₄ O ₂ S			86%	7.8	565.2
646	C ₂₆ H ₂₁ F ₃ N ₄ O ₃ S			88%	7.0	527.2
647	C ₂₆ H ₂₅ F ₃ N ₄ O ₃ S			44+42%	6.59+6.7	531.2



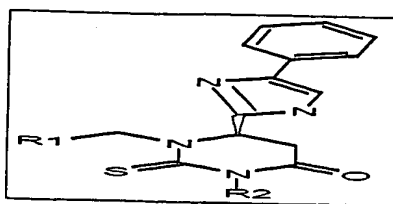
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
648	C ₂₇ H ₂₈ F ₃ N ₅ O ₃ S			81%	5.0	280.8
649	C ₂₈ H ₃₀ F ₃ N ₅ O ₃ S			82%	5.0	287.8
650	C ₂₈ H ₃₂ F ₃ N ₅ O ₂ S			86%	5.2	280.8
651	C ₂₄ H ₂₃ F ₃ N ₄ O ₃ S			90%	6.6	505.2
652	C ₂₅ H ₂₅ F ₃ N ₄ O ₃ S			88%	6.8	519.2



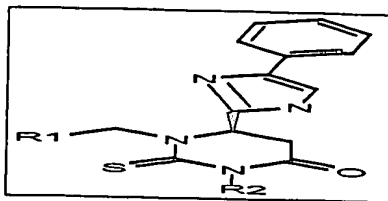
						Analyses	
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺	
653	C29H32N6O3S			88%	6.4	545.3	
654	C30H34N6O3S			90%	6.3	559.3	
655	C31H36N6O3S			89%	6.3	573.3	
656	C32H38N6O3S			91%	6.5	587.3	
657	C33H40N6O3S			91%	6.8	601.3	
658	C25H29N5O3S2			78%	6.7	512.3	
659	C26H31N5O3S2			87%	6.5	526.3	
660	C27H33N5O3S2			86%	6.6	540.3	
661	C28H35N5O3S2			84%	6.8	554.3	
662	C29H37N5O3S2			83%	7.0	568.3	
663	C28H33N5O4S			83%	6.7	536.3	
664	C29H35N5O4S			88%	6.6	550.3	
665	C30H37N5O4S			84%	6.6	564.3	
666	C31H39N5O4S			86%	6.8	578.3	
667	C32H41N5O4S			86%	7.0	592.3	



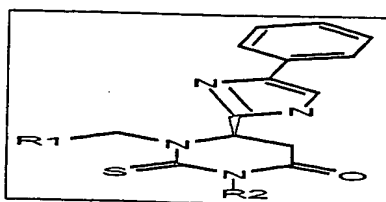
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
668	C29H36N6O3S			82%	5.8	549.3
669	C30H38N6O3S			80%	5.7	563.3
670	C31H40N6O3S			84%	5.8	577.3
671	C32H42N6O3S			84%	6.0	591.4
672	C33H44N6O3S			84%	6.3	605.4
673	C28H30F3N5O4S			82%	7.5	590.3
674	C29H32F3N5O4S			81%	7.3	604.3
675	C30H34F3N5O4S			84%	7.4	618.3
676	C31H36F3N5O4S			86%	7.5	632.3
677	C32H38F3N5O4S			88%	7.7	646.3
678	C29H34N6O4S			81%	5.8	563.3
679	C30H36N6O4S			81%	5.8	577.3
680	C31H38N6O4S			82%	5.8	591.3
681	C32H40N6O4S			82%	6.0	605.3
682	C33H42N6O4S			83%	6.2	619.4



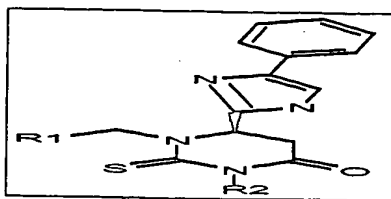
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
683	C ₂₇ H ₃₀ N ₆ O ₅ S			77%	6.9	551.3
684	C ₂₈ H ₃₂ N ₆ O ₅ S			75%	6.8	565.3
685	C ₂₉ H ₃₄ N ₆ O ₅ S			81%	6.9	579.3
686	C ₃₀ H ₃₆ N ₆ O ₅ S			82%	7.0	593.3
687	C ₃₁ H ₃₈ N ₆ O ₅ S			82%	7.3	607.3
688	C ₂₇ H ₃₇ N ₅ O ₃ S			77%	7.5	512.3
689	C ₂₈ H ₃₉ N ₅ O ₃ S			71%	7.3	526.4
690	C ₂₉ H ₄₁ N ₅ O ₃ S			76%	7.3	540.3
691	C ₃₀ H ₄₃ N ₅ O ₃ S			74%	7.5	554.4
692	C ₃₁ H ₄₅ N ₅ O ₃ S			74%	7.7	568.4
693	C ₂₄ H ₂₄ N ₆ O ₅ S			47%	4.2	445.3
694	C ₂₅ H ₂₆ N ₆ O ₅ S			45%	3.9	459.3
695	C ₂₆ H ₂₈ N ₆ O ₅ S			52%	4.0	473.3
696	C ₂₇ H ₃₀ N ₆ O ₅ S			43%	4.1	487.3
697	C ₂₈ H ₃₂ N ₆ O ₅ S			38%	4.3	501.3



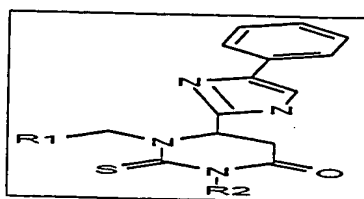
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
698	C ₂₀ H ₂₁ N ₅ O ₂ S ₂			78%	4.1	412.2
699	C ₂₁ H ₂₃ N ₅ O ₂ S ₂			81%	4.0	426.3
700	C ₂₂ H ₂₅ N ₅ O ₂ S ₂			84%	4.1	440.2
701	C ₂₃ H ₂₇ N ₅ O ₂ S ₂			86%	4.2	454.3
702	C ₂₄ H ₂₉ N ₅ O ₂ S ₂			85%	4.3	468.3
703	C ₂₃ H ₂₅ N ₅ O ₂ S			82%	4.2	436.3
704	C ₂₄ H ₂₇ N ₅ O ₂ S			84%	4.1	450.3
705	C ₂₅ H ₂₉ N ₅ O ₂ S			88%	4.2	464.3
706	C ₂₆ H ₃₁ N ₅ O ₂ S			88%	4.3	478.3
707	C ₂₇ H ₃₃ N ₅ O ₂ S			87%	4.4	492.3
708	C ₂₄ H ₂₈ N ₆ O ₂ S			80%	3.5	449.3
709	C ₂₅ H ₃₀ N ₆ O ₂ S			83%	3.4	436.3
710	C ₂₆ H ₃₂ N ₆ O ₂ S			84%	3.5	477.3
711	C ₂₇ H ₃₄ N ₆ O ₂ S			84%	3.6	491.3
712	C ₂₈ H ₃₆ N ₆ O ₂ S			85%	3.8	505.3



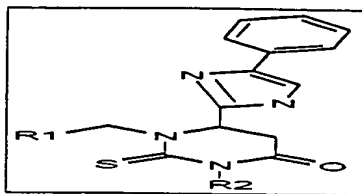
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
713	C23H22F3N5O2S			83%	4.8	490.3
714	C24H24F3N5O2S			84%	4.8	504.2
715	C25H26F3N5O2S			88%	4.8	518.2
716	C26H28F3N5O2S			91%	4.9	532.2
717	C27H30F3N5O2S			90%	5.0	546.2
718	C24H26N6O2S			70%	3.6	463.3
719	C25H28N6O2S			82%	3.5	477.3
720	C26H30N6O2S			83%	3.5	491.3
721	C27H32N6O2S			89%	3.7	505.3
722	C28H34N6O2S			89%	3.8	519.3
723	C22H22N6O3S			81%	4.3	451.2
724	C23H24N6O3S			80%	4.3	465.2
725	C24H26N6O3S			89%	4.3	479.2
726	C25H28N6O3S			86%	4.4	493.3
727	C26H30N6O3S			86%	4.5	507.3



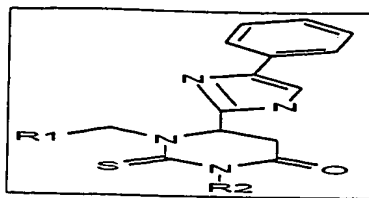
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
728	C ₂₂ H ₂₉ N ₅ O ₂ S			79%	4.8	412.3
729	C ₂₃ H ₃₁ N ₅ O ₂ S			75%	4.6	426.3
730	C ₂₄ H ₃₃ N ₅ O ₂ S			78%	4.6	440.3
731	C ₂₅ H ₃₅ N ₅ O ₂ S			78%	4.7	454.3
732	C ₂₆ H ₃₇ N ₅ O ₂ S			83.8%	5.0	468.2



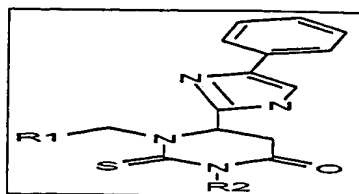
						Analyses	
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺	
733	C ₂₈ H ₂₄ N ₆ O ₂ S			45%	4.7	493.2	
734	C ₂₉ H ₂₆ N ₆ O ₂ S			57%	4.2	507.3	
735	C ₂₄ H ₂₁ N ₅ O ₂ S ₂			69%	4.7	460.2	
736	C ₂₅ H ₂₃ N ₅ O ₂ S ₂			77%	4.2	474.2	
737	C ₂₇ H ₂₅ N ₅ O ₂ S			73%	4.8	484.3	
738	C ₂₈ H ₂₇ N ₅ O ₂ S			76%	4.3	497.3	
739	C ₂₈ H ₂₈ N ₆ O ₂ S			67%	3.9	497.3	
740	C ₂₉ H ₃₀ N ₆ O ₂ S			62%	3.6	511.3	
741	C ₂₇ H ₂₂ F ₃ N ₅ O ₂ S			61%	5.7	538.2	
742	C ₂₈ H ₂₄ F ₃ N ₅ O ₂ S			75%	4.9	552.2	
743	C ₂₈ H ₂₆ N ₆ O ₂ S			57%	4.0	511.2	
744	C ₂₉ H ₂₈ N ₆ O ₂ S			60%	3.7	525.3	
745	C ₂₆ H ₂₂ N ₆ O ₃ S			70%	5.0	499.2	
746	C ₂₇ H ₂₄ N ₆ O ₃ S			65%	4.4	513.2	
747	C ₂₆ H ₂₉ N ₅ O ₂ S			78%	5.4	460.3	



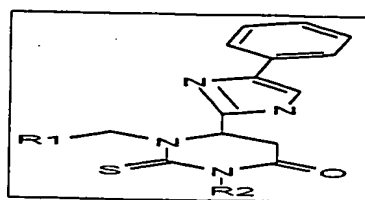
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
748	C27H31N5OS			80%	4.7	474.3
749	C34H34N6O3S			86%	6.6	593.3
750	C33H32N6O3S			82%	6.5	607.3
751	C30H31N5O3S2			77%	6.7	560.2
752	C29H29N5O3S2			77%	6.7	574.2
753	C33H35N5O4S			81%	6.8	584.3
754	C32H33N5O4S			76%	6.7	598.3
755	C34H38N6O3S			77%	5.9	597.3
756	C33H36N6O3S			74%	5.8	611.3
757	C33H32F3N5O4S			76%	7.4	638.3
758	C32H30F3N5O4S			74%	7.3	652.3
759	C34H36N6O4S			78%	6.1	611.3
760	C33H34N6O4S			76%	6.0	625.3
761	C32H32N6O5S			74%	6.9	599.2
762	C31H30N6O5S			69%	6.8	613.3



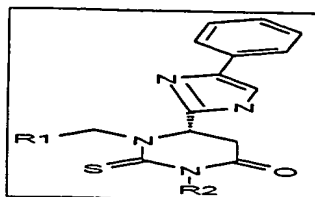
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
763	C32H39N5O3S			78%	7.3	560.3
764	C31H37N5O3S			74%	7.5	574.3
765	C31H34N6O4S			76%	6.9	587.2
766	C32H36N6O4S			86%	6.8	601.3
767	C33H38N6O4S			81%	6.8	615.3
768	C34H40N6O4S			84%	7.0	629.3
769	C35H42N6O4S			78%	7.2	643.4
770	C36H36N6O4S			83%	6.8	649.3
771	C31H34N6O4S			81%	6.9	587.2
772	C32H36N6O4S			76%	6.8	601.3
773	C33H38N6O4S			82%	6.8	615.3
774	C34H40N6O4S			84%	7.0	629.3
775	C35H42N6O4S			73%	7.2	643.3
776	C36H36N6O4S			71%	6.8	649.3
777	C26H26N6O2S			84%	4.4	487.3



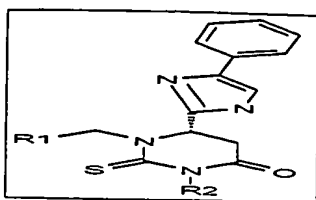
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
778	C ₂₇ H ₂₈ N ₆ O ₂ S			85%	4.4	501.3
779	C ₂₈ H ₃₀ N ₆ O ₂ S			65%	4.4	515.3
780	C ₂₉ H ₃₂ N ₆ O ₂ S			75%	4.6	529.3
781	C ₃₀ H ₃₄ N ₆ O ₂ S			84%	4.7	543.3
782	C ₃₁ H ₂₈ N ₆ O ₂ S			82%	4.5	549.3
783	C ₂₆ H ₂₆ N ₆ O ₂ S			87%	4.4	487.3
784	C ₂₇ H ₂₈ N ₆ O ₂ S			87%	4.4	501.3
785	C ₂₈ H ₃₀ N ₆ O ₂ S			83%	4.4	515.3
786	C ₂₉ H ₃₂ N ₆ O ₂ S			91%	4.5	529.3
787	C ₃₀ H ₃₄ N ₆ O ₂ S			84%	4.7	543.3
788	C ₃₁ H ₂₈ N ₆ O ₂ S			79%	4.5	549.3
789	C ₂₄ H ₂₄ N ₆ O ₂ S			42%	4.3	445.3
790	C ₂₅ H ₂₆ N ₆ O ₂ S			72%	4.1	459.3
791	C ₂₆ H ₂₈ N ₆ O ₂ S			87%	4.1	473.4
792	C ₂₇ H ₃₀ N ₆ O ₂ S			88%	4.3	487.4



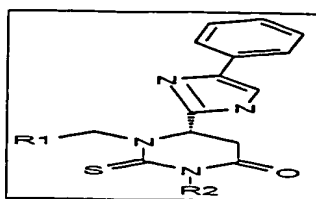
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
793	C ₂₈ H ₃₂ N ₆ O ₂ S	(S)	N	92%	4.4	501.4
794	C ₂₉ H ₂₆ N ₆ O ₂ S	(S)	N	78%	4.3	507.3
795	C ₂₄ H ₂₄ N ₆ O ₂ S	(R)	N	46%	4.3	445.3
796	C ₂₅ H ₂₆ N ₆ O ₂ S	(R)	N	71%	4.1	459.3
797	C ₂₆ H ₂₈ N ₆ O ₂ S	(R)	N	93%	4.1	473.4
798	C ₂₇ H ₃₀ N ₆ O ₂ S	(R)	N	94%	4.3	487.4
799	C ₂₈ H ₃₂ N ₆ O ₂ S	(R)	N	86%	4.5	501.4
800	C ₂₉ H ₂₆ N ₆ O ₂ S	(R)	N	77%		507.3



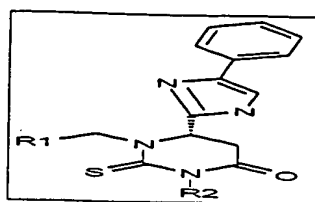
				Analyses		
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
801	C ₃₀ H ₃₀ N ₄ O ₃ S			96%	7.7	495.3
802	C ₃₀ H ₂₉ ClN ₄ O ₃ S			97%	8.1	529.3
803	C ₃₀ H ₂₈ Cl ₂ N ₄ O ₃ S			99%	8.6	563.2
804	C ₃₁ H ₃₂ N ₄ O ₃ S			95%	7.9	509.3
805	C ₃₀ H ₂₉ FN ₄ O ₃ S			96%	7.8	513.3
806	C ₃₁ H ₃₂ N ₄ O ₃ S			93%	7.9	509.3
807	C ₃₁ H ₃₁ ClN ₄ O ₃ S			95%	8.4	543.3
808	C ₃₃ H ₃₆ N ₄ O ₃ S			93%	7.4	569.3
809	C ₃₂ H ₃₄ N ₄ O ₃ S			94%	8.1	523.3
810	C ₂₈ H ₂₈ N ₄ O ₂ S			96%	7.2	485.3
811	C ₂₈ H ₃₂ N ₄ O ₂ S			37+44%	6.7+6.84	489.3
812	C ₂₉ H ₃₅ N ₅ O ₂ S			88%	5.3	518.3
813	C ₃₀ H ₃₇ N ₅ O ₂ S			94%	5.3	532.4
814	C ₃₀ H ₃₉ N ₅ O ₂ S			89%	5.4	518.4
815	C ₂₆ H ₃₀ N ₄ O ₂ S			92%	6.7	463.3



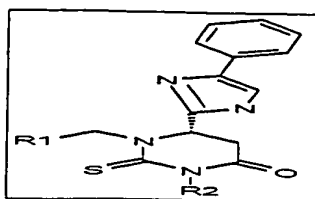
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
816	C ₂₇ H ₃₂ N ₄ O ₂ S			91%	6.9	477.3
817	C ₂₉ H ₂₇ N ₅ O ₂ S			93%	6.0	510.3
818	C ₂₉ H ₂₆ ClN ₅ O ₂ S			87%	6.5	544.2
819	C ₂₉ H ₂₅ Cl ₂ N ₅ O ₂ S			74%	6.9	578.2
820	C ₃₀ H ₂₉ N ₅ O ₂ S			94%	6.2	524.3
821	C ₂₉ H ₂₆ FN ₅ O ₂ S			94%	6.2	528.3
822	C ₃₀ H ₂₉ N ₅ O ₂ S			93%	6.3	524.3
823	C ₃₀ H ₂₈ ClN ₅ O ₂ S			93%	6.7	558.2
824	C ₃₂ H ₃₃ N ₅ O ₄ S			91%	5.7	584.3
825	C ₃₁ H ₃₁ N ₅ O ₂ S			89%	6.5	538.3
826	C ₂₇ H ₂₅ N ₅ O ₃ S			90%	5.5	500.3
827	C ₂₇ H ₂₉ N ₅ O ₃ S			27%+24	4.99+5.1	504.3
828	C ₂₈ H ₃₂ N ₆ O ₃ S			85%	3.9	533.3
829	C ₂₉ H ₃₄ N ₆ O ₃ S			87%	3.9	547.3
830	C ₂₉ H ₃₆ N ₆ O ₂ S			88%	4.1	533.3



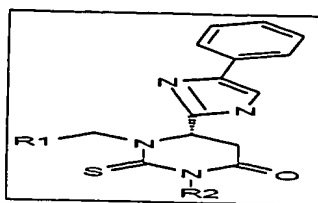
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
831	C ₂₅ H ₂₇ N ₅ O ₃ S			92%	4.9	478.3
832	C ₂₆ H ₂₉ N ₅ O ₃ S			93%	5.1	492.3
833	C ₂₇ H ₂₃ N ₅ O ₃ S			93%	7.0	498.3
834	C ₂₇ H ₂₂ ClN ₅ O ₃ S			85%	7.4	532.2
835	C ₂₇ H ₂₁ Cl ₂ N ₅ O ₃ S			88%	7.8	566.1
836	C ₂₈ H ₂₅ N ₅ O ₃ S			90%	7.3	512.3
837	C ₂₇ H ₂₂ FN ₅ O ₃ S			88%	7.1	516.2
838	C ₂₈ H ₂₅ N ₅ O ₃ S			90%	7.3	512.3
839	C ₂₈ H ₂₄ ClN ₅ O ₃ S			91%	7.8	546.2
840	C ₃₀ H ₂₉ N ₅ O ₅ S			92%	6.8	572.2
841	C ₂₉ H ₂₇ N ₅ O ₃ S			94%	7.5	526.3
842	C ₂₅ H ₂₁ N ₅ O ₄ S			89%	6.6	488.2
843	C ₂₅ H ₂₅ N ₅ O ₄ S			46%+46	6.24+6.4	492.3
844	C ₂₆ H ₂₈ N ₆ O ₄ S			82%	4.6	521.3
845	C ₂₇ H ₃₀ N ₆ O ₄ S			84%	4.6	535.3



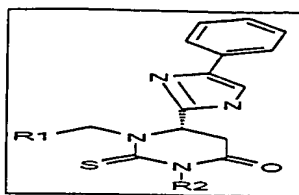
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
846	C27H32N6O3S			76%	4.8	521.3
847	C23H23N5O4S			90%	6.1	466.2
848	C24H25N5O4S			90%	6.3	480.3
849	C24H21N5OS2			87%	6.1	460.2
850	C24H20ClN5OS2			53%	6.6	494.1
851	C24H19Cl2N5OS2			85%	7.0	528.0
852	C25H23N5OS2			79%	6.2	474.1
853	C24H20FN5OS2			76%	6.2	478.1
854	C25H23N5OS2			74%	6.4	474.1
855	C25H22ClN5OS2			82%	6.9	508.1
856	C27H27N5O3S2			73%	5.8	534.1
857	C26H25N5OS2			74%	6.6	488.1
858	C22H19N5O2S2			77%	5.5	450.1
859	C22H23N5O2S2			23+25%	5.2+5.33	454.1
860	C23H26N6O2S2			78%	3.9	483.2



Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
861	C ₂₄ H ₂₈ N ₆ O ₂ S ₂			68%	3.9	497.2
862	C ₂₄ H ₃₀ N ₆ O ₂ S ₂			59%	4.1	483.2
863	C ₂₀ H ₂₁ N ₅ O ₂ S ₂			68%	5.0	428.1
864	C ₂₁ H ₂₃ N ₅ O ₂ S ₂			65%	5.3	442.1
865	C ₂₇ H ₃₀ N ₄ O ₂ S			97%	7.4	459.2
866	C ₂₇ H ₂₉ ClN ₄ O ₂ S			98%	7.9	493.2
867	C ₂₇ H ₂₈ Cl ₂ N ₄ O ₂ S			97%	8.4	527.1
868	C ₂₈ H ₃₂ N ₄ O ₂ S			98%	7.6	473.2
869	C ₂₇ H ₂₉ FN ₄ O ₂ S			96%	7.6	477.2
870	C ₂₈ H ₃₂ N ₄ O ₂ S			94%	7.7	473.2
871	C ₂₈ H ₃₁ ClN ₄ O ₂ S			95%	8.3	507.2
872	C ₃₀ H ₃₆ N ₄ O ₃ S			94%	7.2	533.2
873	C ₂₉ H ₃₄ N ₄ O ₂ S			91%	7.9	487.2
874	C ₂₅ H ₂₈ N ₄ O ₂ S			95%	6.9	449.2
875	C ₂₅ H ₃₂ N ₄ O ₂ S			38+8%	6.9+7.04	453.2

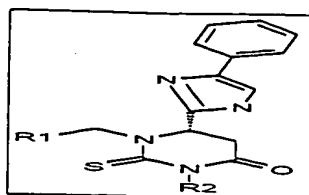


Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
876	C ₂₆ H ₃₅ N ₅ O ₂ S			94%	5.0	482.2
877	C ₂₇ H ₃₇ N ₅ O ₂ S			93%	5.0	496.3
878	C ₂₇ H ₃₉ N ₅ O ₂ S			94%	5.2	482.3
879	C ₂₃ H ₃₀ N ₄ O ₂ S			95%	6.5	427.2
880	C ₂₄ H ₃₂ N ₄ O ₂ S			97%	6.7	441.2

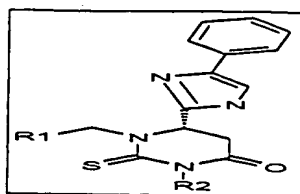


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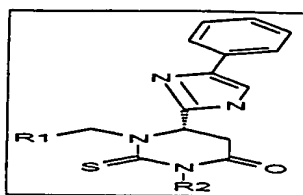
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
881	C ₂₉ H ₂₇ ClN ₄ O ₃ S			78%	7.7	515.2
882	C ₂₉ H ₂₈ N ₄ O ₃ S			59%	7.2	481.2
883	C ₃₁ H ₃₂ N ₄ O ₃ S			63%	8.6	617.2
884	C ₃₁ H ₃₀ N ₄ O ₂ S			61%	7.1	523.2
885	C ₃₂ H ₃₄ N ₄ O ₃ S			60%	7.9	523.3
886	C ₃₁ H ₃₃ N ₅ O ₃ S			28%	6.7	524.2
887	C ₂₉ H ₂₇ N ₅ O ₃ S			53%	7.6	526.2
888	C ₂₉ H ₂₇ BrN ₄ O ₃ S			68%	7.8	559.1
889	C ₂₉ H ₂₆ F ₂ N ₄ O ₃ S			62%	7.3	517.2
890	C ₂₉ H ₂₇ N ₇ O ₃ S			64%	7.6	522.2
891	C ₃₀ H ₂₇ N ₅ O ₃ S			66%	7.3	506.2
892	C ₃₀ H ₂₈ N ₄ O ₃ S			62%	7.1	525.2
893	C ₂₉ H ₂₆ ClN ₅ O ₃ S			55%	7.9	560.1
894	C ₃₃ H ₃₆ N ₄ O ₃ S			59%	8.1	537.3
895	C ₃₀ H ₃₀ N ₄ O ₃ S			67%	7.9	565.2



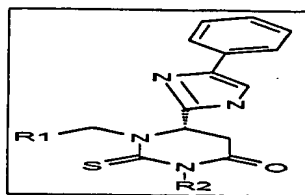
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
896	C ₃₁ H ₃₂ N ₄ O ₂ S			57%	7.7	509.2
897	C ₂₈ H ₂₄ ClN ₅ O ₂ S			64%	6.2	530.1
898	C ₂₈ H ₂₅ N ₅ O ₂ S			64%	5.6	496.2
899	C ₃₀ H ₂₉ N ₅ O ₂ S			52%	7.1	632.2
900	C ₃₀ H ₂₇ N ₅ O ₃ S			57%	5.5	538.2
901	C ₃₁ H ₃₁ N ₅ O ₂ S			65%	6.4	538.2
902	C ₃₀ H ₃₀ N ₆ O ₂ S			29%	5.0	539.2
903	C ₂₈ H ₂₄ N ₆ O ₄ S			51%	6.0	541.2
904	C ₂₈ H ₂₄ BrN ₅ O ₂ S			72%	6.3	574.0
905	C ₂₈ H ₂₃ F ₂ N ₅ O ₂ S			66%	5.7	532.2
906	C ₂₈ H ₂₄ N ₈ O ₂ S			52%	6.1	537.2
907	C ₂₉ H ₂₄ N ₆ O ₂ S			65%	5.7	521.1
908	C ₂₉ H ₂₅ N ₅ O ₄ S			66%	5.5	540.1
909	C ₂₈ H ₂₃ ClN ₆ O ₄ S			55%	6.4	575.1
910	C ₃₂ H ₃₃ N ₅ O ₂ S			64%	6.6	552.2



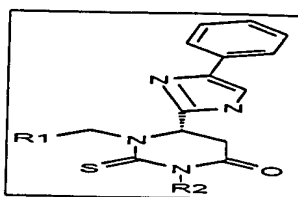
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
911	C ₂₉ H ₂₇ N ₅ O ₂ S			68%	6.5	580.1
912	C ₃₀ H ₂₉ N ₅ O ₂ S			68%	6.1	524.2
913	C ₂₆ H ₂₀ ClN ₅ O ₃ S			60%	7.0	518.1
914	C ₂₆ H ₂₁ N ₅ O ₃ S			63%	6.6	484.2
915	C ₂₈ H ₂₅ N ₅ O ₃ S			41%	7.8	620.1
916	C ₂₈ H ₂₃ N ₅ O ₄ S			51%	6.4	526.1
917	C ₂₉ H ₂₇ N ₅ O ₃ S			64%	7.3	526.2
918	C ₂₈ H ₂₆ N ₆ O ₃ S			21%	6.2	527.2
919	C ₂₆ H ₂₀ N ₆ O ₅ S			27%	6.8	529.1
920	C ₂₆ H ₂₀ BrN ₅ O ₃ S			61%	7.2	562.0
921	C ₂₆ H ₁₉ F ₂ N ₅ O ₃ S			55%	6.6	520.1
922	C ₂₆ H ₂₀ N ₈ O ₃ S			61%	7.0	525.1
923	C ₂₇ H ₂₀ N ₆ O ₃ S			50%	6.6	509.1
924	C ₂₇ H ₂₁ N ₅ O ₅ S			68%	6.5	528.1
925	C ₂₆ H ₁₉ ClN ₆ O ₅ S			44%	7.2	563.1



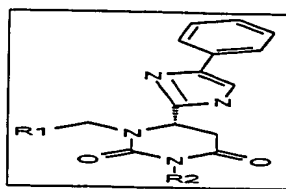
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
926	C30H29N5O3S			60%	7.5	540.2
927	C27H23N5O3S			62%	7.3	568.1
928	C28H25N5O3S			60%	7.0	512.2
929	C23H18ClN5OS2			28%	6.4	480.1
930	C23H19N5OS2			22%	5.8	446.1
931	C25H23N5OS2			34%	7.3	582.1
932	C25H21N5O2S2			25%	5.7	488.1
933	C26H25N5OS2			21%	6.6	488.1
934	C25H24N6OS2			13%	5.3	489.1
935	C23H18N6O3S2			23%	6.2	491.1
936	C23H18BrN5OS2			38%	6.5	524.0
937	C23H17F2N5OS2			58%	5.8	482.1
938	C23H18N8OS2			28%	6.3	487.1
939	C24H18N6OS2			32%	5.9	471.1
940	C24H19N5O3S2			23%	5.7	490.1



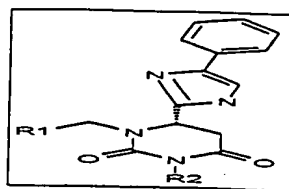
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
941	C23H17ClN6O3S2			33%	6.7	525.0
942	C27H27N5OS2			29%	6.8	502.2
943	C24H21N5OS2			35%	6.7	530.1
944	C25H23N5OS2			16%	6.3	474.1
945	C26H27ClN4OS			61%	7.5	479.2
946	C26H28N4OS			54%	7.0	445.2
947	C28H32N4OS			61%	8.4	581.1
948	C28H30N4O2S			49%	6.9	487.2
949	C29H34N4OS			57%	7.7	487.2
950	C28H33N5OS			16%	6.4	488.2
951	C26H27N5O3S			44%	7.4	490.2
952	C26H27BrN4OS			70%	7.6	523.1
953	C26H26F2N4OS			61%	7.0	481.2
954	C26H27N7OS			66%	7.4	486.2
955	C27H27N5OS			68%	7.1	470.2



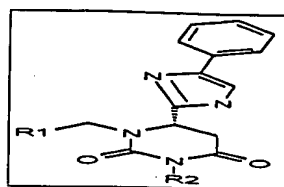
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
956	C ₂₇ H ₂₈ N ₄ O ₃ S			63%	6.9	489.2
957	C ₂₆ H ₂₆ ClN ₅ O ₃ S			66%	7.7	524.1
958	C ₃₀ H ₃₆ N ₄ O ₃ S			58%	7.9	501.3
959	C ₂₇ H ₃₀ N ₄ O ₃ S			64%	7.7	529.2
960	C ₂₈ H ₃₂ N ₄ O ₃ S			46%	7.5	473.2



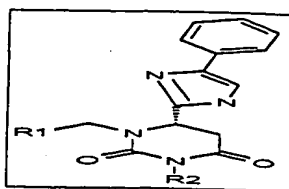
				Analyses		
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
961	C30H30N4O3			57%	10.5	495.2
962	C30H27F3N4O2			69%	11.6	533.2
963	C29H28N4O2			69%	10.4	465.2
964	C29H27N5O4			61%	11.0	510.2
965	C30H29ClN4O2			74%	11.6	513.2
966	C32H32N4O4			52%	11.0	537.2
967	C29H27BrN4O2			76%	11.2	543.1
968	C29H27FN4O2			60%	10.7	483.2
969	C29H26Cl2N4O2			68%	11.9	533.1
970	C31H30N4O3			71%	10.3	507.2
971	C30H30N4O2S			72%	10.9	511.2
972	C30H27F3N4O3			77%	11.6	549.2
973	C29H27BrN4O2			66%	11.3	543.1
974	C32H34N4O2			85%	11.5	507.3
975	C29H26F2N4O2			72%	10.8	501.2



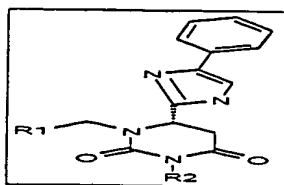
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
976	C ₃₂ H ₃₄ N ₄ O ₅			71%	10.3	555.2
977	C ₂₉ H ₂₇ N ₅ O ₄			72%	8.0	510.2
978	C ₂₉ H ₂₄ F ₃ N ₅ O ₃			70%	9.3	548.2
979	C ₂₈ H ₂₅ N ₅ O ₃			79%	7.8	480.2
980	C ₂₈ H ₂₄ N ₆ O ₅			62%	8.6	525.2
981	C ₂₉ H ₂₆ ClN ₅ O ₃			71%	9.1	528.2
982	C ₃₁ H ₂₉ N ₅ O ₅			65%	8.6	552.2
983	C ₂₈ H ₂₄ BrN ₅ O ₃			82%	8.8	558.1
984	C ₂₈ H ₂₄ FN ₅ O ₃			73%	8.2	498.2
985	C ₂₈ H ₂₃ Cl ₂ N ₅ O ₃			66%	9.5	548.1
986	C ₃₀ H ₂₇ N ₅ O ₄			81%	7.7	522.2
987	C ₂₉ H ₂₇ N ₅ O ₃ S			79%	8.4	526.2
988	C ₂₉ H ₂₄ F ₃ N ₅ O ₄			83%	9.3	564.2
989	C ₂₈ H ₂₄ BrN ₅ O ₃			69%	8.8	558.1
990	C ₃₁ H ₃₁ N ₅ O ₃			84%	9.2	522.3



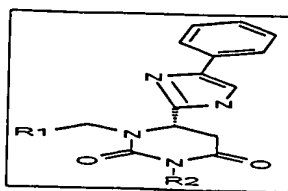
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
991	C ₂₈ H ₂₃ F ₂ N ₅ O ₃			86%	8.1	516.2
992	C ₃₁ H ₃₁ N ₅ O ₆			60%	7.7	570.2
993	C ₂₇ H ₂₃ N ₅ O ₅			76%	9.5	498.2
994	C ₂₇ H ₂₀ F ₃ N ₅ O ₄			71%	10.7	536.1
995	C ₂₆ H ₂₁ N ₅ O ₄			85%	9.4	468.2
996	C ₂₆ H ₂₀ N ₆ O ₆			56%	10.0	513.2
997	C ₂₇ H ₂₂ ClN ₅ O ₄			77%	10.7	516.1
998	C ₂₉ H ₂₅ N ₅ O ₆			64%	10.2	540.2
999	C ₂₆ H ₂₀ BrN ₅ O ₄			83%	10.4	546.0
1000	C ₂₆ H ₂₀ FN ₅ O ₄			74%	9.8	486.2
1001	C ₂₆ H ₁₉ Cl ₂ N ₅ O ₄			69%	11.0	536.1
1002	C ₂₈ H ₂₃ N ₅ O ₅			81%	9.3	510.2
1003	C ₂₇ H ₂₃ N ₅ O ₄ S			79%	10.1	514.1
1004	C ₂₇ H ₂₀ F ₃ N ₅ O ₅			74%	10.8	552.1
1005	C ₂₆ H ₂₀ BrN ₅ O ₄			66%	10.4	546.0



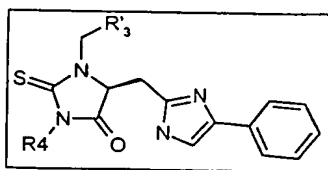
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
1006	C ₂₉ H ₂₇ N ₅ O ₄			84%	10.8	510.2
1007	C ₂₆ H ₁₉ F ₂ N ₅ O ₄			76%	9.8	504.1
1008	C ₂₉ H ₂₇ N ₅ O ₇			74%	9.3	558.2
1009	C ₂₄ H ₂₁ N ₅ O ₃ S			60%	8.2	460.1
1010	C ₂₄ H ₁₈ F ₃ N ₅ O ₂ S			65%	9.5	498.1
1011	C ₂₃ H ₁₉ N ₅ O ₂ S			77%	8.0	430.1
1012	C ₂₃ H ₁₈ N ₆ O ₄ S			60%	8.7	475.1
1013	C ₂₄ H ₂₀ ClN ₅ O ₂ S			62%	9.4	478.1
1014	C ₂₆ H ₂₃ N ₅ O ₄ S			63%	8.9	502.2
1015	C ₂₃ H ₁₈ BrN ₅ O ₂ S			79%	9.1	508.0
1016	C ₂₃ H ₁₈ FN ₅ O ₂ S			63%	8.4	448.1
1017	C ₂₃ H ₁₇ Cl ₂ N ₅ O ₂ S			54%	9.8	498.1
1018	C ₂₅ H ₂₁ N ₅ O ₃ S			82%	8.0	472.1
1019	C ₂₄ H ₂₁ N ₅ O ₂ S ₂			73%	8.8	476.1
1020	C ₂₄ H ₁₈ F ₃ N ₅ O ₃ S			70%	9.6	514.1



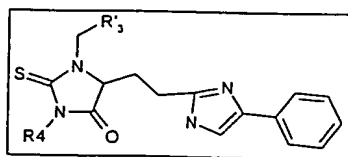
Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
1021	C ₂₃ H ₁₈ BrN ₅ O ₂ S			60%	9.2	508.0
1022	C ₂₆ H ₂₅ N ₅ O ₂ S			74%	9.6	472.2
1023	C ₂₃ H ₁₇ F ₂ N ₅ O ₂ S			62%	8.3	466.1
1024	C ₂₆ H ₂₅ N ₅ O ₅ S			64%	8.0	520.1
1025	C ₂₇ H ₂₂ F ₂ N ₄ O ₃			76%	9.4	489.2
1026	C ₂₇ H ₁₉ F ₅ N ₄ O ₂			77%	10.6	527.1
1027	C ₂₆ H ₂₀ F ₂ N ₄ O ₂			87%	9.2	459.2
1028	C ₂₆ H ₁₉ F ₂ N ₅ O ₄			79%	9.9	504.1
1029	C ₂₇ H ₂₁ ClF ₂ N ₄ O ₂			74%	10.6	507.1
1030	C ₂₉ H ₂₄ F ₂ N ₄ O ₄			59%	10.1	531.2
1031	C ₂₆ H ₁₉ BrF ₂ N ₄ O ₂			82%	10.3	537.1
1032	C ₂₆ H ₁₉ F ₃ N ₄ O ₂			79%	9.7	477.1
1033	C ₂₆ H ₁₈ Cl ₂ F ₂ N ₄ O ₂			69%	11.0	527.1
1034	C ₂₈ H ₂₂ F ₂ N ₄ O ₃			82%	9.2	501.2
1035	C ₂₇ H ₂₂ F ₂ N ₄ O ₂ S			76%	9.9	505.1



Ex. No.	Formula	R1	R2	Purity	rt (min)	[M+H] ⁺
1036	C ₂₇ H ₁₉ F ₅ N ₄ O ₃			83%	10.7	543.1
1037	C ₂₆ H ₁₈ BrF ₂ N ₄ O ₂			68%	10.4	537.1
1038	C ₂₉ H ₂₆ F ₂ N ₄ O ₂			86%	10.7	501.2
1039	C ₂₆ H ₁₈ F ₄ N ₄ O ₂			80%	9.6	495.1
1040	C ₂₉ H ₂₆ F ₂ N ₄ O ₅			43%	9.2	549.2

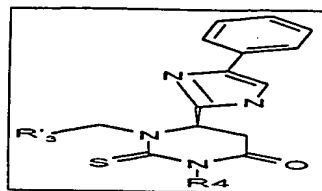


						Analyses	
Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺	
1041	C ₂₆ H ₃₃ N ₅ O S ₂			56	3.69	496.3	
1042	C ₂₉ H ₃₇ N ₅ O ₂ S			74	3.78	520.3	
1043	C ₃₀ H ₃₆ N ₆ O S			76	3.77	529.3	
1044	C ₃₁ H ₃₈ N ₆ O S			73	3.85	543.3	
1045	C ₃₀ H ₃₉ N ₅ O S			63	4.19	518.3	
1046	C ₃₀ H ₃₆ N ₆ O S			71	4.01	529.3	

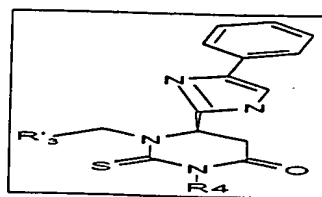


Analyses

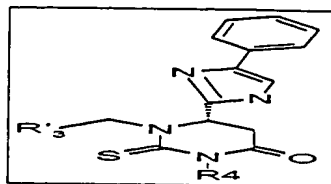
Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1047	C ₂₇ H ₃₅ N ₅ O S ₂			69	3.65	510.3
1048	C ₃₀ H ₃₉ N ₅ O ₂ S			75	3.75	534.3
1049	C ₃₁ H ₄₂ N ₆ O S			71	3.49	547.3
1050	C ₃₁ H ₃₈ N ₆ O S			66	3.74	543.3
1051	C ₃₁ H ₃₈ N ₆ O S			87	3.89	543.3



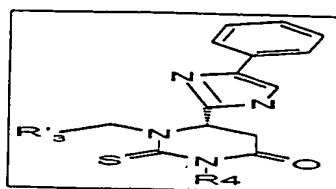
Ex. No.	Formula	R ³	R ⁴	Analyses		
				Purity	rt (min)	[M+H] ⁺
1052	C ₃₀ H ₃₆ N ₆ O S			83.38	4.71	529.3
1053	C ₂₆ H ₃₃ N ₅ O S ₂			72.31	4.41	496.3
1054	C ₂₉ H ₃₇ N ₅ O ₂ S			71.47	4.5	520.3
1055	C ₃₀ H ₄₀ N ₆ O S			62.38	3.86	533.3
1056	C ₂₅ H ₃₂ N ₆ O S ₂			25.6	3.9	497.2
1057	C ₂₈ H ₃₃ F ₂ N ₅ O S			63.2	4.5	526.3
1058	C ₃₁ H ₄₁ N ₅ O S			69.01	5.17	532.4
1059	C ₂₈ H ₃₄ N ₆ O ₃ S			73.01	4.58	535.3
1060	C ₂₈ H ₄₁ N ₅ O S			44.6	4.9	496.4
1061	C ₂₉ H ₃₄ F ₃ N ₅ O ₂ S			80.9	5.1	574.2
1062	C ₃₀ H ₃₉ N ₅ O S			58.64	4.91	518.3
1063	C ₃₆ H ₄₂ N ₆ O S			54.23	5.3	607.3
1064	C ₂₈ H ₃₄ Br N ₅ O S			76.51	4.86	568.2
1065	C ₂₈ H ₃₃ Cl ₂ N ₅ O S			74.91	5.03	558.2
1066	C ₂₉ H ₃₄ F ₃ N ₅ O S			66.26	4.93	558.2



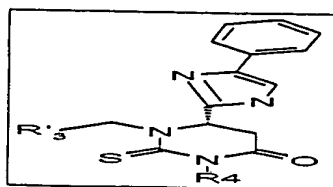
Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1067	C ₂₈ H ₃₄ N ₆ O ₃ S			40	4.6	535.2
1068	C ₃₂ H ₃₇ N ₅ O S			73.1	4.9	540.3
1069	C ₂₉ H ₃₄ N ₆ O ₅ S			55.8	4.58	579.2
1070	C ₃₄ H ₃₉ N ₅ O S			64.6	5.2	566.3
1071	C ₂₉ H ₃₄ N ₆ O S			70.75	4.38	515.3
1072	C ₂₉ H ₃₇ N ₅ O S			64.36	4.68	504.3
1073	C ₃₅ H ₄₁ N ₅ O ₂ S			40.5	5	596.3
1074	C ₃₁ H ₃₈ N ₆ O S			80.4	4	543.3



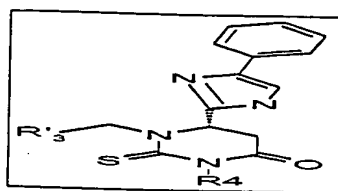
				Analyses		
Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1075	C ₂₆ H ₃₂ N ₆ O ₃ S ₂			45.2%	6.1	541.3
1076	C ₂₇ H ₃₄ N ₆ O ₃ S ₂			35.3%	6.3	555.3
1077	C ₂₈ H ₃₆ N ₆ O ₃ S ₂			39.9%	6.5	569.3
1078	C ₃₀ H ₃₈ N ₆ O ₃ S ₂			14.9+22.82%	6,7+6,76	595.3
1079	C ₃₂ H ₄₁ N ₅ O ₃ S			70.3%	7.5	576.4
1080	C ₃₃ H ₄₃ N ₅ O ₃ S			71.9%	7.7	590.4
1081	C ₃₄ H ₄₅ N ₅ O ₃ S			72.7%	7.9	604.4
1082	C ₃₆ H ₄₇ N ₅ O ₃ S			34.6+34.7%	8.1+8.28	630.4
1083	C ₂₉ H ₃₃ F ₂ N ₅ O ₃ S			60.6%	6.9	570.3
1084	C ₃₀ H ₃₅ F ₂ N ₅ O ₃ S			62.7%	7.1	584.3
1085	C ₃₁ H ₃₇ F ₂ N ₅ O ₃ S			65.5%	7.3	598.3
1086	C ₃₃ H ₃₉ F ₂ N ₅ O ₃ S			33.92%+32.4%	7.5+4.6	624.3
1087	C ₂₉ H ₃₄ BrN ₅ O ₃ S			65.6%	7.3	612.2
1088	C ₃₀ H ₃₆ BrN ₅ O ₃ S			68.6%	7.5	626.2
1089	C ₃₁ H ₃₈ BrN ₅ O ₃ S			75.2%	7.7	640.3



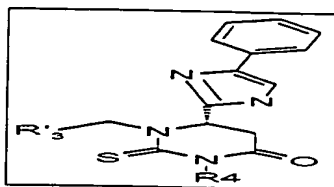
Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1090	C ₃₃ H ₄₀ BrN ₅ O ₃ S			37.14%+37.1%	7.88+8.0	666.3
1091	C ₂₉ H ₃₄ BrN ₅ O ₃ S			71.9%	7.3	612.2
1092	C ₃₀ H ₃₆ BrN ₅ O ₃ S			76.2%	7.4	626.2
1093	C ₃₁ H ₃₈ BrN ₅ O ₃ S			77.0%	7.6	640.3
1094	C ₃₃ H ₄₀ BrN ₅ O ₃ S			39.4+39.64%	7.8+8.0	666.3
1095	C ₂₉ H ₃₃ Cl ₂ N ₅ O ₃ S			72.1%	7.6	602.2
1096	C ₃₀ H ₃₅ Cl ₂ N ₅ O ₃ S			74.9%	7.7	616.3
1097	C ₃₁ H ₃₇ Cl ₂ N ₅ O ₃ S			76.4%	7.9	630.3
1098	C ₃₃ H ₃₉ Cl ₂ N ₅ O ₃ S			39.6%+39.16%	8.1+8.4	656.3
1099	C ₃₀ H ₃₄ F ₃ N ₅ O ₃ S			64.3%	7.3	602.3
1100	C ₃₁ H ₃₆ F ₃ N ₅ O ₃ S			71.3%	7.5	616.3
1101	C ₃₂ H ₃₈ F ₃ N ₅ O ₃ S			71.6%	7.6	630.3
1102	C ₃₄ H ₄₀ F ₃ N ₅ O ₃ S			34.8+34.91%	8.0+7.8	656.4
1103	C ₂₉ H ₃₄ N ₆ O ₅ S			63.2%	6.9	579.3
1104	C ₃₀ H ₃₆ N ₆ O ₅ S			66.1%	7.1	593.3



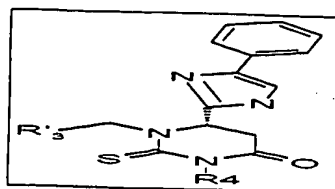
Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1105	C ₃₁ H ₃₈ N ₆ O ₅ S			66.1%	7.3	607.3
1106	C ₃₃ H ₄₀ N ₆ O ₅ S			33.7%+24.4%	7.5+7.6	633.4
1107	C ₃₃ H ₃₇ N ₅ O ₃ S			84.0%	7.2	584.4
1108	C ₃₄ H ₃₉ N ₅ O ₃ S			86.3%	7.4	598.4
1109	C ₃₅ H ₄₁ N ₅ O ₃ S			86.2%	7.6	612.4
1110	C ₃₇ H ₄₃ N ₅ O ₃ S			43.1%+43.4%	7.9+8.12	638.4
1111	C ₃₆ H ₄₁ N ₅ O ₄ S			58.2%	7.3	640.4
1112	C ₃₇ H ₄₃ N ₅ O ₄ S			61.1%	7.5	654.4
1113	C ₃₈ H ₄₅ N ₅ O ₄ S			67.6%	7.7	668.4
1114	C ₄₀ H ₄₇ N ₅ O ₄ S			38.1%+38.5%	7.9+8.1	694.4
1115	C ₂₁ H ₂₄ N ₆ O ₂ S			74.0%	3.9	441.2
1116	C ₂₂ H ₂₆ N ₆ O ₂ S			80.2%	4.0	455.3
1117	C ₂₃ H ₂₈ N ₆ O ₂ S			47.3%	4.2	469.3
1118	C ₂₅ H ₃₀ N ₆ O ₂ S			18.31%+14%	4.2+4.3	495.3
1119	C ₂₇ H ₃₃ N ₅ O ₂ S			76.8%	5.1	476.4



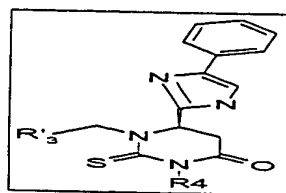
Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1120	C ₂₈ H ₃₅ N ₅ O ₅			77.9%	5.3	490.4
1121	C ₂₉ H ₃₇ N ₅ O ₅			75.6%	5.4	504.4
1122	C ₃₁ H ₃₉ N ₅ O ₅			38.42%+26.7% ^m	5.5+5.7	530.4
1123	C ₂₄ H ₂₅ F ₂ N ₅ O ₅			68.1%	4.5	470.3
1124	C ₂₅ H ₂₇ F ₂ N ₅ O ₅			66.9%	4.7	484.3
1125	C ₂₆ H ₂₉ F ₂ N ₅ O ₅			70.0%	4.8	498.3
1126	C ₂₈ H ₃₁ F ₂ N ₅ O ₅			25.0%	4.9	524.3
1127	C ₂₄ H ₂₆ BrN ₅ O ₅			72.7%	4.9	512.2
1128	C ₂₅ H ₂₈ BrN ₅ O ₅			78.5%	5.0	526.2
1129	C ₂₆ H ₃₀ BrN ₅ O ₅			80.2%	5.1	540.2
1130	C ₂₈ H ₃₂ BrN ₅ O ₅			39.21%+27%	5.3+5.4	566.2
1131	C ₂₄ H ₂₆ BrN ₅ O ₅			77.9%	4.9	512.2
1132	C ₂₅ H ₂₈ BrN ₅ O ₅			81.4%	5.0	526.2
1133	C ₂₆ H ₃₀ BrN ₅ O ₅			78.25% [*]	5.1	540.2
1134	C ₂₈ H ₃₂ BrN ₅ O ₅			31.02%+27.9	5.2+5.4	566.2



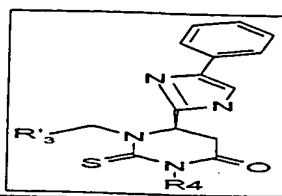
Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1135	C ₂₄ H ₂₅ Cl ₂ N ₅ OS			79.9%	5.1	502.2
1136	C ₂₅ H ₂₇ Cl ₂ N ₅ OS			81.2%	5.2	516.2
1137	C ₂₆ H ₂₉ Cl ₂ N ₅ OS			80.1%	5.3	530.2
1138	C ₂₈ H ₃₁ Cl ₂ N ₅ OS			33.63%+28.8%	5.4+5.6	556.2
1139	C ₂₅ H ₂₆ F ₃ N ₅ OS			73.7%	4.9	502.3
1140	C ₂₆ H ₂₈ F ₃ N ₅ OS			80.8%	5.1	516.2
1141	C ₂₇ H ₃₀ F ₃ N ₅ OS			76.86%*	5.2	530.3
1142	C ₂₉ H ₃₂ F ₃ N ₅ OS			27.7%+27.3	5.3+5.4	556.3
1143	C ₂₄ H ₂₆ N ₆ O ₃ S			70.7%	4.6	479.3
1144	C ₂₅ H ₂₈ N ₆ O ₃ S			72.3%	4.7	493.3
1145	C ₂₆ H ₃₀ N ₆ O ₃ S			72.4%	4.8	507.3
1146	C ₂₈ H ₃₂ N ₆ O ₃ S			27.5%+26.5%	4.9+5.3	533.3
1147	C ₂₈ H ₂₉ N ₅ OS			88.2%	4.8	484.3
1148	C ₂₉ H ₃₁ N ₅ OS			89.1%	5.0	498.3
1149	C ₃₀ H ₃₃ N ₅ OS			89.9%	5.1	512.3



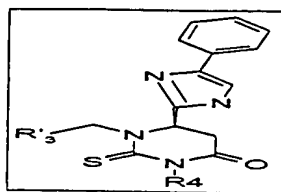
Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1150	C ₃₂ H ₃₅ N ₅ O ₂ S			46.67%+31.0	5.3+5.5	538.3
1151	C ₃₁ H ₃₃ N ₅ O ₂ S			46.0%	5.0	540.3
1152	C ₃₂ H ₃₅ N ₅ O ₂ S			46.6%	5.1	554.2
1153	C ₃₃ H ₃₇ N ₅ O ₂ S			54.2%	5.2	568.3
1154	C ₃₅ H ₃₉ N ₅ O ₂ S			28+21%	5.3+5.5	594.3



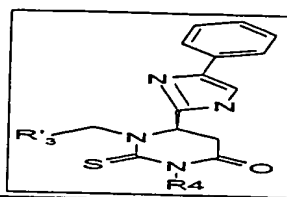
						Analyses	
Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺	
1155	C ₂₉ H ₃₄ N ₆ O ₅ S			82%	6.5	579.3	
1156	C ₃₀ H ₃₆ N ₆ O ₅ S			85%	6.7	593.3	
1157	C ₃₁ H ₃₈ N ₆ O ₅ S			84%	6.9	607.4	
1158	C ₃₃ H ₄₀ N ₆ O ₅ S			42+42%	7.1+7.28	633.4	
1159	C ₃₀ H ₃₄ N ₆ O ₇ S			78%	6.5	623.3	
1160	C ₃₀ H ₃₆ N ₆ O ₇ S			82%	6.7	637.3	
1161	C ₃₂ H ₃₈ N ₆ O ₇ S			80%	6.9	651.3	
1162	C ₃₄ H ₄₀ N ₆ O ₇ S			34+41%	7.1+7.2	677.4	
1163	C ₃₅ H ₃₉ N ₅ O ₃ S			83%	7.1	610.4	
1164	C ₃₆ H ₄₁ N ₅ O ₃ S			84%	7.3	624.4	
1165	C ₃₇ H ₄₃ N ₅ O ₃ S			85%	7.5	638.4	
1166	C ₃₉ H ₄₅ N ₅ O ₃ S			41+42%	7.7+7.9	664.4	
1167	C ₃₃ H ₃₇ N ₅ O ₃ S			91%	6.9	584.4	
1168	C ₃₄ H ₃₉ N ₅ O ₃ S			90%	7.1	598.4	
1169	C ₃₅ H ₄₁ N ₅ O ₃ S			89%	7.3	612.4	



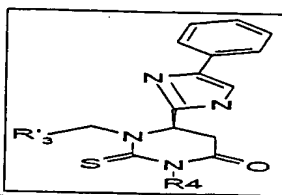
Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1170	C ₃₇ H ₄₃ N ₅ O ₃ S			41+42%	7.5+7.7	638.4
1171	C ₃₀ H ₃₄ N ₆ O ₃ S			85%	6.4	559.3
1172	C ₃₁ H ₃₆ N ₆ O ₃ S			87%	6.5	573.3
1173	C ₃₂ H ₃₈ N ₆ O ₃ S			81%	6.8	587.4
1174	C ₃₄ H ₄₀ N ₆ O ₃ S			42+43%	6.9+7.1	613.4
1175	C ₃₇ H ₄₃ N ₅ O ₅ S			86%	6.9	670.4
1176	C ₃₈ H ₄₅ N ₅ O ₅ S			82%	7.1	684.5
1177	C ₃₉ H ₄₇ N ₅ O ₅ S			86%	7.3	698.5
1178	C ₄₁ H ₄₉ N ₅ O ₅ S			38.3+38.4%	7.5+7.62	724.4
1179	C ₃₁ H ₃₉ N ₅ O ₃ S			86%	6.9	562.4
1180	C ₃₂ H ₄₁ N ₅ O ₃ S			87%	7.1	576.4
1181	C ₃₃ H ₄₃ N ₅ O ₃ S			86%	7.3	590.4
1182	C ₃₅ H ₄₅ N ₅ O ₃ S			38+39%	7.5+7.64	616.4
1183	C ₃₇ H ₄₂ N ₆ O ₃ S			85%	7.2	651.4
1184	C ₃₈ H ₄₄ N ₆ O ₃ S			88%	7.3	665.4



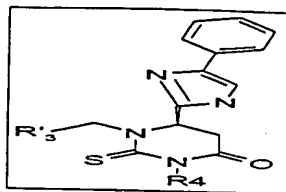
Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1185	C ₃₉ H ₄₆ N ₆ O ₃ S			88%	7.5	679.4
1186	C ₄₁ H ₄₈ N ₆ O ₃ S			38.4+38.5%	7.8+7.98	705.4
1187	C ₃₆ H ₃₉ N ₅ O ₃ S			86%	7.2	622.4
1188	C ₃₇ H ₄₁ N ₅ O ₃ S			87%	7.4	636.4
1189	C ₃₈ H ₄₃ N ₅ O ₃ S			82%	7.6	650.4
1190	C ₄₀ H ₄₅ N ₅ O ₃ S			40.6+40.9%	7.8+8.01	676.4
1191	C ₃₁ H ₃₆ N ₆ O ₃ S			85.41%*	6.6	573.3
1192	C ₃₂ H ₃₈ N ₆ O ₃ S			89%	6.8	587.4
1193	C ₃₃ H ₄₀ N ₆ O ₃ S			90%	7.0	601.4
1194	C ₃₅ H ₄₂ N ₆ O ₃ S			43.1+44.5%	7.3+7.45	627.4
1195	C ₂₄ H ₂₆ N ₆ O ₃ S			87%	4.3	479.3
1196	C ₂₅ H ₂₈ N ₆ O ₃ S			92%	4.4	493.3
1197	C ₂₆ H ₃₀ N ₆ O ₃ S			92%	4.6	507.3
1198	C ₂₈ H ₃₂ N ₆ O ₃ S			35+33.9%	4.7+4.8	533.3
1199	C ₂₅ H ₂₆ N ₆ O ₅ S			82%	4.3	523.2



Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1200	C ₂₆ H ₂₈ N ₆ O ₅ S			86%	4.5	537.3
1201	C ₂₇ H ₃₀ N ₆ O ₅ S			83%	4.6	551.3
1202	C ₂₉ H ₃₂ N ₆ O ₅ S			35+33.9%	4.7+4.8	577.3
1203	C ₃₀ H ₃₁ N ₅ O ₅ S			88%	4.9	510.3
1204	C ₃₁ H ₃₃ N ₅ O ₅ S			90%	5.0	524.3
1205	C ₃₂ H ₃₅ N ₅ O ₅ S			89%	5.2	538.3
1206	C ₃₄ H ₃₇ N ₅ O ₅ S			43+31%	5.3+5.4	564.3
1207	C ₂₈ H ₂₉ N ₅ O ₅ S			92%	4.7	484.3
1208	C ₂₉ H ₃₁ N ₅ O ₅ S			93%	4.8	498.3
1209	C ₃₀ H ₃₃ N ₅ O ₅ S			92%	4.9	512.3
1210	C ₃₂ H ₃₅ N ₅ O ₅ S			43+30.1%	5.1	538.3
1211	C ₂₅ H ₂₆ N ₆ O ₅ S			87%	4.1	459.3
1212	C ₂₆ H ₂₈ N ₆ O ₅ S			86%	4.2	473.3
1213	C ₂₇ H ₃₀ N ₆ O ₅ S			82%	4.4	487.3
1214	C ₂₉ H ₃₂ N ₆ O ₅ S			40+36%	4.5+4.6	513.3



Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1215	C ₃₂ H ₃₅ N ₅ O ₃ S			87%	4.8	570.3
1216	C ₃₃ H ₃₇ N ₅ O ₃ S			84%	4.9	584.3
1217	C ₃₄ H ₃₉ N ₅ O ₃ S			86%	5.0	598.3
1218	C ₃₆ H ₄₁ N ₅ O ₃ S			32%+29%	5.2+5.3	624.4
1219	C ₂₆ H ₃₁ N ₅ O ₃ S			90%	4.6	462.3
1220	C ₂₇ H ₃₃ N ₅ O ₃ S			92%	4.7	476.4
1221	C ₂₈ H ₃₅ N ₅ O ₃ S			91%	4.9	490.4
1222	C ₃₀ H ₃₇ N ₅ O ₃ S			42+29.9%	5.0+5.2	516.3
1223	C ₃₂ H ₃₄ N ₆ O ₃ S			80%	5.0	551.3
1224	C ₃₃ H ₃₆ N ₆ O ₃ S			90%	5.1	565.3
1225	C ₃₄ H ₃₈ N ₆ O ₃ S			85%	5.3	579.4
1226	C ₃₆ H ₄₀ N ₆ O ₃ S			37%+27	5.45.6	605.4
1227	C ₃₁ H ₃₁ N ₅ O ₃ S			90%	5.0	522.3
1228	C ₃₂ H ₃₃ N ₅ O ₃ S			91%	5.1	536.3
1229	C ₃₃ H ₃₅ N ₅ O ₃ S			90%	5.2	550.3



Ex. No.	Formula	R ³	R ⁴	Purity	rt (min)	[M+H] ⁺
1230	C ₃₅ H ₃₇ N ₅ O ₂ S			42%+30.8	5.4+5.5	576.3
1231	C ₂₆ H ₂₈ N ₆ O ₂ S			68%	4.4	473.4
1232	C ₂₇ H ₃₀ N ₆ O ₂ S			56%	4.5	487.4
1233	C ₂₈ H ₃₂ N ₆ O ₂ S			40%	4.7	613.2
1234	C ₃₀ H ₃₄ N ₆ O ₂ S			40%	4.8	527.4

PHARMACOLOGICAL PROPERTIES OF THE COMPOUNDS OF THE INVENTION

The compounds of the present invention can and have been tested as regards their affinity for different sub-types of somatostatin receptors according to the procedures described below.

Study of the affinity for the sub-types of human somatostatin receptors:

The affinity of a compound of the invention for sub-types of somatostatin receptors 1 to 5 (sst_1 , sst_2 , sst_3 , sst_4 and sst_5 , respectively) is determined by measurement of the inhibition of the bond of [^{125}I -Tyr 11]SRIF-14 to transfected CHO-K1 cells.

10 The gene of the sst_1 receptor of human somatostatin has been cloned in the form of a genomic fragment. A segment *Pst*I-*Xmn*I of 1.5 Kb containing 100 bp of the non transcribed 5' region, 1.17 Kb of the coding region in totality, and 230 bp of the non transcribed 3' region is modified by the addition of the linker BglIII. The resulting DNA fragment is subcloned in the *Bam*HI site of a pCMV-81 in order to produce the
15 expression plasmid in mammals (provided by Dr. Graeme Bell, Univ. Chicago). A cloned cell line expressing in a stable fashion the sst_1 receptor is obtained by transfection in CHO-K1 cells (ATCC) using the calcium phosphate co-precipitation method. The plasmid pRSV-neo (ATCC) is included as selection marker. Cloned cell lines were selected in an RPMI 1640 medium containing 0.5 mg/ml of G418 (Gibco),
20 followed by circular cloning and multiplication in culture.

The gene of the sst_2 receptor of human somatostatin, isolated in the form of a genomic fragment of DNA of 1.7 Kb *Bam*HI-*Hind*III and subcloned in a plasmid vector pGEM3Z (Promega), was provided by Dr. G. Bell (Univ. of Chicago). The expression vector of the mammalian cells is constructed by inserting the *Bam*HI-*Hind*II fragment
25 of 1.7 Kb in endonuclease restriction sites compatible with the plasmid pCMV5. A cloned cell line is obtained by transfection in CHO-K1 cells using the calcium phosphate co-precipitation method. The plasmid pRSV-neo is included as selection marker.

The sst_3 receptor is isolated as a genomic fragment, and the complete coding sequence is
30 contained in a *Bam*HI/*Hind*III fragment of 2.4 Kb. The expression plasmid in mammals, pCMV-h3, is constructed by insertion of the *Nco*I-*Hind*III fragment of

2.0 Kb in the EcoR1 site of the vector pCMV after modification of the terminations and addition of EcoR1 linkers. A cloned cell line expressing in a stable fashion the sst₃ receptor is obtained by transfection in CHO-K1 cells (ATCC) by the calcium phosphate co-precipitation method. The plasmid pRSV-neo (ATCC) is included as selection marker. Cloned cell lines were selected in an RPMI 1640 medium containing 0.5 mg/ml of G418 (Gibco), followed by circular cloning and multiplication in culture.

The expression plasmid of the human sst₄ receptor, pCMV-HX, was provided by Dr. Graeme Bell (Univ. Chicago). This vector contains the genomic fragment coding for the human sst₄ receptor of 1.4 Kb *NheI-NheI*, 456 pb of the non transcribed 5' region, and 200 pb of the non transcribed 3' region, cloned in the *XbaI/EcoR1* sites of PCMV-HX. A cloned cell line expressing in a stable fashion the sst₄ receptor is obtained by transfection in CHO-K1 cells (ATCC) by the calcium phosphate co-precipitation method. The plasmid pRSV-neo (ATCC) is included as selection marker. The cloned cell lines were selected in an RPMI 1640 medium containing 0.5 mg/ml of G418 (Gibco), followed by circular cloning and multiplication in culture.

The gene corresponding to the human sst₃ receptor, obtained by the PCR method using a genomic clone as probe, was provided by Dr. Graeme Bell (Univ. Chicago). The resulting PCR fragment of 1.2 Kb contains 21 base pairs of the non transcribed 5' region, the coding region in totality, and 55 pb of the non transcribed 3' region. The clone is inserted in an EcoR1 site of the plasmid pBSSK(+). The insert is recovered in the form of a *HindIII-XbaI* fragment of 1.2 Kb for subcloning in an expression vector in mammals, pCVM5. A cloned cell line expressing in a stable fashion the sst₃ receptor is obtained by transfection in CHO-K1 cells (ATCC) by the calcium phosphate co-precipitation method. The plasmid pRSV-neo (ATCC) is included as selection marker. The cloned cell lines were selected in an RPMI 1640 medium containing 0.5 mg/ml of G418 (Gibco), followed by circular cloning and multiplication in culture.

The CHO-K1 cells which express in a stable fashion the human sst receptors are cultured in an RPMI 1640 medium containing 10% of foetal calf serum and 0.4 mg/ml of geneticin. The cells are collected with 0.5 mM EDTA and centrifuged at 500 g for approximately 5 minutes at approximately 4°C. The pellet is resuspended in Tris 50 mM at pH 7.4 and centrifuged twice at 500 g for approximately 5 minutes at approximately 4°C. The cells are lysed by sonication and centrifuged at 39000 g for approximately 10 minutes at 4°C. The pellet is resuspended in the same buffer and centrifuged at 50000 g for approximately 10 minutes at approximately 4°C and the membranes in the pellet obtained are stored at -80°C.

The competitive inhibition tests of the bond with [^{125}I -Tyr 11]SRIF-14 are carried out in duplicate using 96-well polypropylene plates. The cell membranes (10 μg protein/well) are incubated with [^{125}I -Tyr 11]SRIF-14 (0.05 nM) for approximately 60 min. at approximately 37 °C in a 50 mM HEPES buffer (pH 7.4) containing BSA 0.2 %, MgCl_2 5 mM, Trasylol 200 KIU/ml, bacitracin 0.02 mg/ml, phenylmethylsulphonyl fluoride 0.02 mg/ml.

The bound [^{125}I -Tyr 11]SRIF-14 is separated from the free [^{125}I -Tyr 11]SRIF-14 by immediate filtration through GF/C glass fibre filter plates (Unifilter, Packard) pre-impregnated with 0.1 % of polyethylenimine (P.E.I.), using a Filtermate 196 (Packard). The filters are washed with 50 mM HEPES buffer at approximately 0-4 °C for approximately 4 seconds and their radioactivity is determined using a counter (Packard Top Count).

The specific bond is obtained by subtracting the non-specific bond (determined in the presence of 0.1 μM of SRIF-14) from the total bond. The data relative to the bond are analyzed by computer-aided non-linear regression analysis (MDL) and the values of the inhibition constants (K_i) are determined.

Determination of the agonist or antagonist character of a compound of the present invention is carried out using the test described below.

Functional test: Inhibition of production of intracellular cAMP:

CHO-K1 cells expressing the sub-types of human somatostatin receptors (SRIF-14) are cultured in 24-well plates in an RPMI 1640 medium with 10% of foetal calf serum and 0.4 mg/ml of geneticin. The medium is changed the day preceding the experiment.

The cells at a rate of 10^5 cells/well are washed twice with 0.5 ml of new RPMI medium comprising 0.2 % BSA completed by 0.5 mM of 3-isobutyl-1-methylxanthine (IBMX) and incubated for approximately 5 min at approximately 37 °C.

The production of cyclic AMP is stimulated by the addition of 1 mM of forskolin (FSK) for 15-30 minutes at approximately 37 °C.

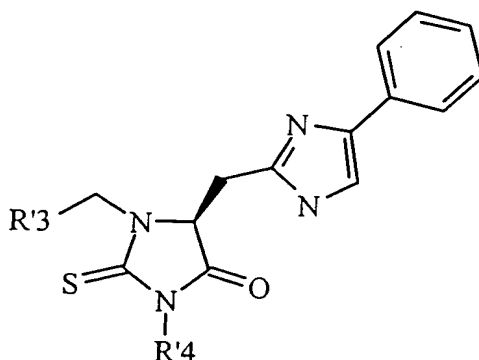
The inhibitor effect of the somatostatin of an agonist compound is measured by the simultaneous addition of FSK (1 μM), SRIF-14 (10^{-12} M to 10^{-6} M) and of the compound to be tested (10^{-10} M to 10^{-5} M).

The antagonist effect of a compound is measured by the simultaneous addition of FSK (1 μ M), SRIF-14 (1 to 10 nM) and of the compound to be tested (10⁻¹⁰ M to 10⁻⁵ M).

The reaction medium is eliminated and 200 ml of 0.1 N HCl are added. The quantity of cAMP is measured by a radioimmunological test (FlashPlate SMP001A kit, New England Nuclear).

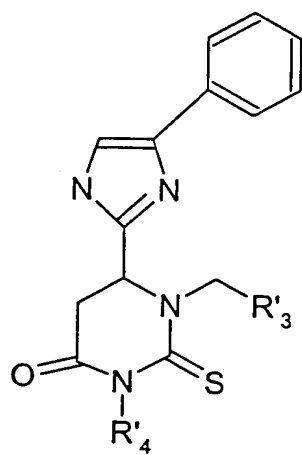
Results:

The tests carried out according to the protocols described above have demonstrated that the compounds of general formula (I) defined in the present Application have a good affinity for at least one of the sub-types of somatostatin receptors, the inhibition constant K_i being lower than micromolar for certain exemplified compounds, and in particular for the compounds shown in the Tables I and II below.



R'3	R'4	K_i
	$(CH_2)_3NH_2$	< 1 μ M
	$(CH_2)_4NH_2$	< 1 μ M
	$(CH_2)_5NH_2$	< 1 μ M
	$(CH_2)_6NH_2$	< 1 μ M
	$(CH_2)_3NH_2$	< 1 μ M
	$(CH_2)_4NH_2$	< 1 μ M
	$(CH_2)_5NH_2$	< 1 μ M
	$(CH_2)_6NH_2$	< 1 μ M

TABLE I



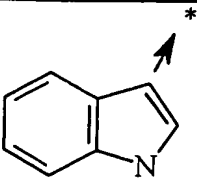
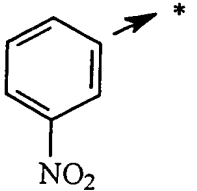
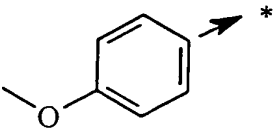
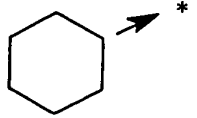
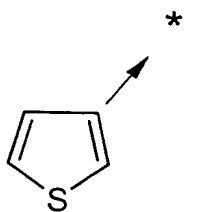
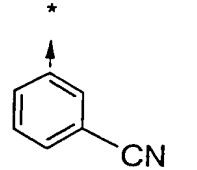
R'3	R'4	K _i
	$(CH_2)_4NH_2$ $(CH_2)_5NH_2$ $(CH_2)_6NH_2$ $(CH_2)_6NMe_2$	$< 1\mu M$ $< 1\mu M$ $< 1\mu M$
	$(CH_2)_5NH_2$ $(CH_2)_6NH_2$ $(CH_2)_6NMe_2$	$< 1\mu M$ $< 1\mu M$ $< 1\mu M$
	$(CH_2)_5NH_2$ $(CH_2)_6NH_2$ $(CH_2)_6NMe_2$	$< 1\mu M$ $< 1\mu M$ $< 1\mu M$
	$(CH_2)_5NH_2$ $(CH_2)_6NH_2$ $(CH_2)_6NMe_2$	$< 1\mu M$ $< 1\mu M$ $< 1\mu M$
	$(CH_2)_5NH_2$ $(CH_2)_6NH_2$ $(CH_2)_6NMe_2$	$< 1\mu M$ $< 1\mu M$ $< 1\mu M$
	$(CH_2)_6NMe_2$	$< 1\mu M$

TABLE II